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Base-induced reactions of p-Nitrobenzyl compounds

Paul Henry Ruehle

Department: Chemistry

BASE-INDUCED REACTIONS OF p-NITROBENZYL COMPOUNDS

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Samuel J. Havens
Advisor
B Ken Robertson
Robert R Russell

James Stoffer
J C Wolf

ABSTRACT

The base-induced reactions of several p-nitrobenzyl compounds were studied. The products varied with changes in the leaving groups. With relatively poor leaving groups (Cl, $\overset{+}{S}(Me)_2$), p,p'-dinitrostilbene was produced in good yield. The products of the reaction of p-nitrobenzyl chloride and hydroxide ion in 50% aqueous dioxane were 52.0% p,p'-dinitrostilbene, 43.9% cis- and trans-p,p'-dinitrostilbene oxides, 3.2% p-nitrobenzyl alcohol, and traces of other compounds. With dissolved oxygen, no stilbene was produced; the main product was 88% cis- and trans-p,p'-dinitrostilbene oxides. The addition of small amounts of di-t-butyl nitroxide caused a decrease in both the rate of the reaction and the amount of the stilbene produced. Larger amounts (40 mol%) completely inhibited the formation of the stilbene. Oxygen and di-t-butyl nitroxide had similar but smaller effects on the reaction of both p-nitrobenzyldimethylsulfonium bromide and tosylate. Compounds with good leaving groups (Br, I, Ots) gave only small amounts of the stilbene; instead, the major product was the corresponding alcohol. For p-nitrobenzyl bromide, the major product was not p,p'-dinitrobibenzyl ether, as previously reported; 4.8% of the ether, and 66.7% p-nitrobenzyl alcohol were found.

Deuterium and chlorine kinetic isotope effects were determined for the reaction of p-nitrobenzyl chloride. In addition to the previously suggested alkylation-dehydrohalogenation and α-elimination mechanisms, a radical anion mechanism is proposed.

ACKNOWLEDGEMENTS

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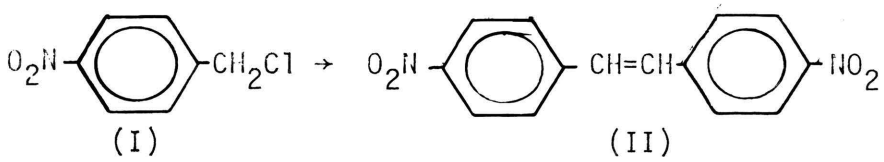
I. INTRODUCTION

The hydrolysis of benzyl chlorides in neutral or acidic solutions was studied extensively by Olivier from the early 20's to mid 30's.[1] He showed that the hydrolysis occurs by a unimolecular process (S_N1), and that the rate of chloride ion liberation is retarded by <u>meta</u> and <u>para</u> electron-withdrawing substituents on the ring.[1]

(1)

With nucleophiles stronger than water, the chloride displacement is more complicated. Studies by Olivier on the alkaline hydrolysis of benzyl chlorides,[2a] by Beste and Hammett on displacement by hydroxide and acetate ions,[2b] and by Simonetta and Favini on the alkaline hydrolysis of benzyl, o-, m-, and p-methoxybenzyl chlorides,[2c] all point to the operation of both uni- and bi-molecular processes (S_N1 and S_N2) concurrently. Thirty years after Olivier's proposition concerning the simultaneous operation of nucleophile-assisted and nucleophile-independent processes, Hill and Fry established a correlation between the magnitude of the chlorine kinetic isotope effect (k^{35}/k^{37}) and the extent of the S_N1 and S_N2 processes in the displacements on benzyl chlorides.[3]

Of all the benzyl chlorides studied by Olivier, only p-nitrobenzyl chloride (I) did not undergo the expected hydrolysis in a basic medium to yield the alcohol, presumably because it underwent preferentially an eliminative condensation to yield p,p'-dinitrostilbene (II), eq 2.



(I) (II) (2)

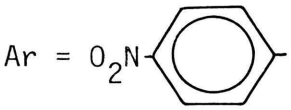
The formation of (II) was not suspected by Olivier in 1934, but was reported as the product of the above transformation as early as 1890 by Walden and Kernbaum.[4*] The formation of (II) from (I) in alcoholic KOH is paralleled by the formation of stilbene from benzyl chloride and sodamide in liquid ammonia.[5]

In 1929, Bergmann and Hervey offered to explain the I→II transformation by postulating a divalent carbon intermediate that dimerizes to form the dinitrostilbene.[6]

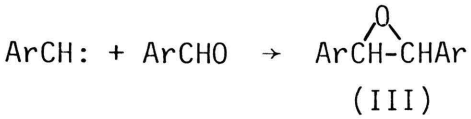
$$ArCH_2Cl + OH^- \rightarrow Ar\dot{C}HCl + H_2O \quad (3a)$$

$$Ar\dot{C}HCl \rightarrow ArCH: + Cl^- \quad (3b)$$

$$2\ ArCH: \rightarrow ArCH{=}CHAr \quad (3c)$$



Their attempt to trap the proposed intermediate with p-nitrobenzaldehyde gave a mixture of <u>cis</u>- and <u>trans</u>-p,p'-dinitrostilbene oxides (eq 4) as predicted.[6]



(III)

<u>cis</u> and <u>trans</u> (4)

*Three components were isolated from the crude precipitate: a "high melting form" of the dinitrostilbene, mp 280-285° (from nitrobenzene), a "low melting form" of the dinitrostilbene, mp 210-216° (from chloroform), and a third component, mp 165-175° (from benzene).

The divalent carbon hypothesis was challenged by Kleucker, who proposed that the epoxides were formed from a chlorohydrin intermediate, and not from an attack of a divalent species on p-nitrobenzaldehyde.[7]

$$ArCH_2Cl + OH^- \rightarrow Ar\bar{C}HCl + H_2O \qquad (5a)$$

$$ArCHCl + ArCHO \rightarrow \left[ArCH(O^-)-CHAr \; (Cl) \right] \rightarrow (III) \qquad (5b)$$

Hann also criticized the hypothesis of Bergmann and Hervey, and suggested an alkylation-dehydrohalogenation mechanism for the formation of p,p'-dinitrostilbene.[8]

$$ArCH_2Cl + OH^- \rightarrow Ar\bar{C}HCl + H_2O \qquad (6a)$$

$$Ar\bar{C}HCl + ArCH_2Cl \rightarrow ArCH_2CHClAr + Cl^- \qquad (6b)$$

$$ArCH_2CHClAr + OH^- \rightarrow ArCH{=}CHAr + H_2O + Cl^- \qquad (6c)$$

In 1961, a kinetic study revealed that the carbanion of (I) and not the divalent species, reacts with p-nitrobenzaldehyde (eq 5b) to form a mixture of <u>cis</u>- and <u>trans</u>-p,p'-dinitrostilbene oxides (III).[9] The rate of chloride ion liberation in the p-nitrobenzyl chloride--hydroxide ion reaction was significantly increased in the presence of p-nitrobenzaldehyde. This, however, did not seem to rule out the

possibility of radicals or divalent species in the formation of p,p'-dinitrostilbene.[9]

The kinetics of the reaction of (I) with sodium hydroxide in 50% aqueous dioxane were studied by following the rate of the release of chloride ion; it is first order in (I) and first order in hydroxide ion.[9]

$$\text{Rate} = k\,[ArCH_2Cl]\cdot[OH^-] \tag{7}$$

The first step, a proton abstraction, was shown to be reversible by tracer studies. A kinetic isotope effect, $k_H/k_D = 1.28$, was observed for p-nitrobenzyl chloride (66% deuterium in the side chain).[9] Since the kinetics seemed to rule out an alkylation-dehydrohalogenation mechanism (eq 6a-6c), which should be a third order reaction, the authors proposed the following mechanism.

$$ArCH_2Cl + OH^- \rightleftarrows Ar\bar{C}HCl + H_2O \tag{8a}$$

$$Ar\bar{C}HCl \xrightarrow{rds} ArCH: + Cl^- \tag{8b}$$

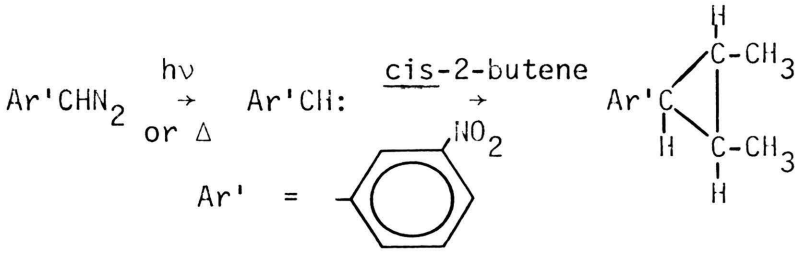
$$2\ ArCH: \rightarrow ArCH{=}CHAr \tag{8c}$$

$$\underline{\text{or}}\ ArCH: + Ar\bar{C}HCl \rightarrow Ar\bar{C}HCHClAr \tag{8d}$$

$$Ar\bar{C}HCHClAr \rightarrow ArCH{=}CHAr + Cl^- \tag{8e}$$

Paths 8c and 8d-8e cannot be distinguished kinetically, since they occur after the rate-determining step (8b).[9]

Attempts to trap the proposed carbene intermediate with cyclohexene, employing conditions that are known to yield the stilbene (II), were unsuccessful.[10] However, m-nitrophenyl carbene, generated from the corresponding diazo compound, has been trapped with cis-2-butene (eq 9) and other olefins to yield cyclopropanes.[11]



(9)

The absence of side products in the reactions which presumably involved p-nitrophenyl carbene was attributed to the selectivity of the proposed carbene and its reaction with the conjugate base of (I) rather than hydroxide ion[12] or other species.[13]

An alkylation-dehydrohalogenation mechanism was suggested for the formation of p,p'-dinitrostilbene from p-nitrobenzyl chloride and methoxide ion in DMSO--methanol mixtures.[14] This mechanism was favored by Tommila because the α-chlorobibenzyl intermediate ($ArCH_2CHClAr$) has been isolated for the reaction of other benzyl halides with alkali amides in liquid ammonia,[15] and that p-nitrobenzyl chloride reacts with cyanide ion in DMSO to give p,p'-dinitrostilbene.[16]

In a study of other p-nitrobenzyl compounds, it was reported that the reactions of p-nitrobenzyl bromide and p-nitrobenzyl iodide with sodium hydroxide in 50% aqueous dioxane do not give p,p'-dinitrostilbene, but p,p'-dinitrobibenzyl ether (eq 10) in quantitative yield.[17]

$$ArCH_2X + OH^- \rightleftarrows Ar\bar{C}HX + H_2O \quad (10a)$$

$$ArCH_2X + OH^- \xrightarrow{rds} ArCH_2OH + X^- \quad (10b)$$

$$ArCH_2OH + OH^- \xrightarrow{rapid} ArCH_2O^- + H_2O \quad (10c)$$

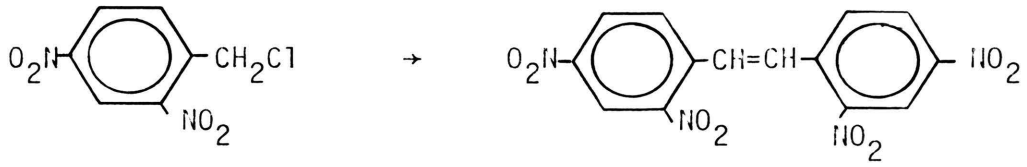
$$ArCH_2O^- + ArCH_2X \xrightarrow{rapid} ArCH_2OCH_2Ar + X^- \quad (10d)$$

$$X = Br \text{ or } I$$

The carbanions from these halides are formed more rapidly than the corresponding carbanion from (I), as evidenced by their more rapid conversion to p,p'-dinitrostilbene oxides (III) in the presence of p-nitrobenzaldehyde. However, in the absence of p-nitrobenzaldehyde, the rate of reaction of these two halides is slower than the corresponding chloride. The absence of stilbene formation in these cases was attributed to the inability of the bromide ion (or iodide ion) to separate from the carbanion, presumably due to d-orbital stabilization.[17]

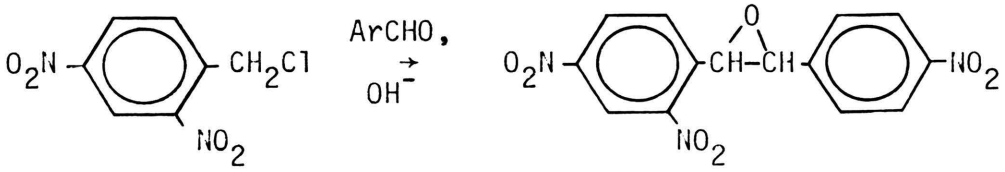
The halide displacement reactions of a series of substituted benzyl fluorides were studied in both acidic and basic media.[18] p-Nitrobenzyl fluoride is the slowest to hydrolyze in aqueous ethanol, but reacts the fastest in basic ethanolic solutions; a highly colored solution and a solid melting above 300 degrees was obtained.[18] This indicated that the reaction was not a simple displacement of fluoride by ethoxide ion.[18]

2,4-Dinitrobenzyl chloride rapidly forms 2,2',4,4'-tetranitrostilbene (eq 11) in alcoholic alkali,[19] or with hydroxide ion in aqueous dioxane.[9]



(11)

The behavior of this halide in the presence of added p-nitrobenzaldehyde is identical to that of p-nitrobenzyl chloride; the product with p-nitrobenzaldehyde and potassium carbonate in methanol is 2,4,4'-trinitrostilbene oxide.[9]



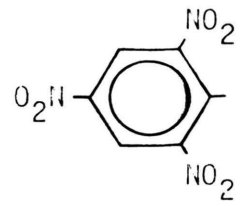
(12)

An alkylation-dehydrohalogenation mechanism (eq 13) has been proposed for the transformation of 2,4,6-trinitrobenzyl chloride in basic media to the corresponding stilbene.[20]

$$Ar'CH_2Cl + OH^- \rightarrow Ar'\bar{C}HCl + H_2O \quad (13a)$$

$$Ar'\bar{C}HCl + Ar'CH_2Cl \rightarrow Ar'CH_2CHClAr' + Cl^- \quad (13b)$$

$$Ar'CH_2CHClAr' + OH^- \rightarrow Ar'CH{=}CHAr' + H_2O + Cl^- \quad (13c)$$

Ar' = 

The yield of the stilbene is optimum, 50% of the theoretical yield, for a 1:1 mole ratio of the halide to NaOH.[20] With insufficient amounts of sodium hydroxide, unreacted chloride was recovered; however, with excess sodium hydroxide, no unreacted chloride was recovered, but a red-brown amorphous material was isolated showing at least 12 components by thin layer chromatography.[20] No stilbene was isolated for a 1:2 ratio; this was attributed to the high acidity of the benzylic hydrogen. Presumably, with excess base, essentially none of the neutral molecule would be present for the carbanion to attack; only the side reactions would be possible, giving the amorphous material. The authors ruled out a carbene mechanism, as they found no difference in the products with added cyclohexene.[20]

Swain and Thornton studied the reactions of various substituted benzyldimethylsulfonium salts in aqueous base, and reported that p-nitrobenzyldimethylsulfonium tosylate (IV) gave 99% cis- and trans-p,p'-dinitrostilbene;[12] other substituted benzyldimethylsulfonium ions gave only the corresponding alcohols in high yields.[21] It is significant that m-nitrobenzyldimethylsulfonium ion also gave none of the corresponding dinitrostilbene.[22] The parallelism of the reaction of (IV) and hydroxide ion to the p-nitrobenzyl chloride case is striking; the kinetics are first order in each reactant, and the

first step of the reaction was shown by tracer studies to be a reversible proton abstraction. The sulfur isotope effect, k_{32}/k_{34} = 1.0066 ± 0.0008, is too low for a mechanism protraying stilbene formation only through the dimerization of two carbenes, but is reasonable for the attack of a carbene on the ylide, followed by rapid loss of dimethylsulfide to give the product (II).[12]

$$ArCH_2\overset{+}{S}(Me)_2 + OH^- \rightleftarrows Ar\overset{-}{C}H\overset{+}{S}(Me)_2 + H_2O \qquad (14a)$$

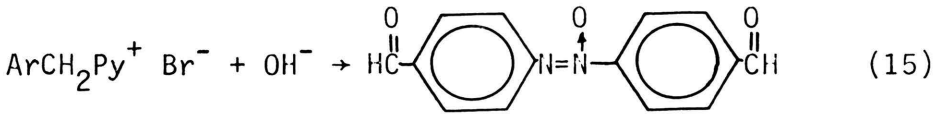
$$Ar\overset{-}{C}H\overset{+}{S}(Me)_2 \xrightarrow{rds} ArCH: + S(Me)_2 \qquad (14b)$$

$$ArCH: + Ar\overset{-}{C}H\overset{+}{S}(Me)_2 \rightarrow \left[Ar\overset{-}{C}HCHAr \;\; \overset{+}{S}(Me)_2 \right] \rightarrow ArCH{=}CHAr \quad (II) \qquad (14c)$$

Further work on various p-nitrobenzylsulfonium salts shows that the nature of the leaving group affects the products in a dramatic way.[13] p-Nitrobenzyl alcohol and trans-p,p'-dinitrostilbene oxide, as well as the stilbene (II), were isolated by column chromatography from the reaction products of p-nitrobenzylmethylisopropylsulfonium ion (and other p-nitrobenzylsulfonium ions) with base.[13] The stilbene oxide was shown to arise from oxygen in the solvent. The mixture of products was attributed to the greater steric hindrance involved in the attack of the proposed p-nitrophenyl carbene on the ylide; the ylide of the dimethylsulfonium salt is less hindered than that of the methylisopropylsulfonium salt, and presumably the carbene could

attack it exclusively and no other species.[13] In the more hindered case, the carbene is less selective; presumably it reacts with oxygen and hydroxide ion (or water) to form the observed p,p'-dinitrostilbene oxide and p-nitrobenzyl alcohol.[13]

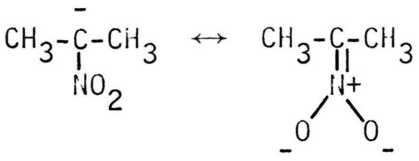
The reaction of p-nitrobenzylpyridinium bromide with sodium hydroxide was studied by Hanna, to see if it would react in a manner similar to the sulfonium salts. The product was shown to be p-azoxybenzaldehyde (eq 15); no p,p'-dinitrostilbene was detected.[23]



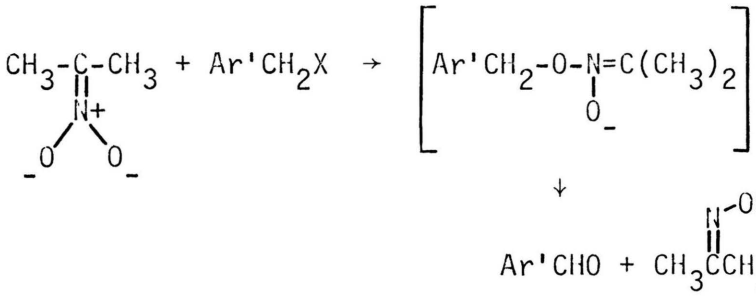
(15)

Alkaline hydrolysis of certain p-nitrobenzyl thioethers has been shown to yield the same azoxy-compound.[24]

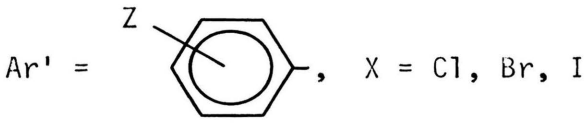
In a study of the reaction of alkylating agents with carbanions of nitroalkanes, p-nitrobenzyl chloride was found to show unusual behavior.[25] Other substituted benzyl halides react with the lithium salt of 2-nitropropane (2-nitro-2-propyl anion) to yield the corresponding substituted benzaldehyde, the O-alkylated product.[25] The carbanion acts as an ambident nucleophile, and reacts with most substituted benzyl halides to form an unstable nitronic ester. The ester is not isolated, but gives the substituted benzaldehyde and acetoxime.[25]



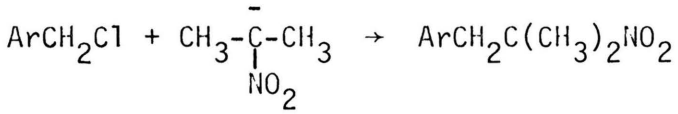
(16a)



(16b)



However, with p-nitrobenzyl chloride, the predominant product is 2-methyl-2-nitro-2-(p-nitrophenyl)propane (eq 17), the C-alkylated product.[25]



(17)

C-alkylation depends not only on the substituents on the ring, but also on the leaving group; p-nitrobenzyl bromide and p-nitrobenzyl iodide give mostly the O-alkylated product, and p-nitrobenzyl tosylate is intermediate in behavior.[26]

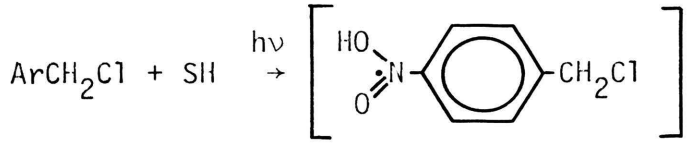
Table I

Products from p-Nitrobenzyl Halides ($ArCH_2X$) and 2-Nitro-2-propyl Anion in Ethanol[26]

Leaving Group	C-alkylation	O-alkylation
X = Cl	95%	1%
X = OTs	40%	32%
X = Br	17%	65%
X = I	9%	81%

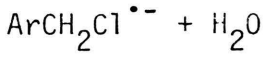
It is noteworthy that in 1949, Hass and Bender noticed a parallelism between the ability of o-nitro, p-nitro, and 2,4-dinitrobenzyl chlorides to undergo C-alkylation with 2-nitro-2-propyl anion, and their ability to form the corresponding stilbene in alcoholic sodium hydroxide or sodium alkoxide.[27]

Some C-alkylated product is formed with all the nitrobenzyl halides studied, presumably by an S_N2 process.[28] However, the large amount of C-alkylation observed for p-nitrobenzyl chloride in the absence of electron acceptors indicates that in this case, C-alkylation occurs by more than one pathway; it is postulated that the predominant pathway involves radicals.[28] p-Nitrobenzyl chloride radical anion (V), a proposed intermediate, would decay by loss of a chloride ion to give p-nitrobenzyl radical (VI).[28,29]

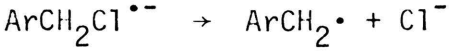


(19a)

SH = protic solvent ↓ OH^-

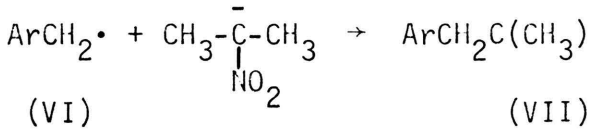


(V)



(19b)

In ethanol, no C-alkylation occurs without illumination; however, in dimethylformamide, the reaction proceeds in the dark, but at a slower rate.[29] Although the radical anion (V) was not observed during C-alkylation, presumably due to its instability, the ESR signal of the product radical ion (VII) was observed.[29] It is postulated that the radical (VI) couples with 2-nitro-2-propyl anion (eq 20), to give the radical ion (VII).[29]



(20)

The product radical ion (VII) then decays by a one-electron transfer to p-nitrobenzyl chloride, giving the C-alkylated product, and another radical anion (V), in a chain propagating step.[29]

$$(VII) + ArCH_2Cl \rightarrow ArCH_2C(CH_3)_2NO_2 + (V) \qquad (21)$$

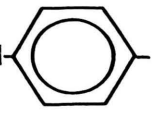
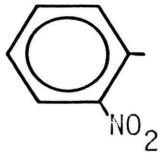
The radical anion (V), as well as other nitrobenzyl halo radical anions, have been generated electrochemically.[30] The o- and p-nitrobenzyl halides gave both the corresponding bibenzyl (the dimer) and the nitrotoluene.[30]

$$Ar'CH_2X + e^- \rightarrow Ar'CH_2X^{\bullet -} \qquad (22a)$$

$$Ar'CH_2X^{\bullet -} \rightarrow Ar'CH_2\bullet + X^- \qquad (22b)$$

$$Ar'CH_2\bullet + SH \rightarrow Ar'CH_3 + S\bullet \qquad (22c)$$

$$2\ Ar'CH_2\bullet \rightarrow Ar'CH_2CH_2Ar' \qquad (22d)$$

Ar' =  or  X = Cl, Br, I

The m-nitrobenzyl halides gave only m-nitrotoluene.[30]

The nature of the radical pathway for C-alkylation has been further clarified by studying the reaction p-nitrobenzyl chloride and 2-nitro-2-propyl anion in the presence of m- and p-dinitrobenzenes; the amount of C-alkylation was greatly reduced by these compounds.[28] Similar results were obtained with p-nitrobenzyl chloride and the sodium salt of 2-carbethoxycoumaran-2-one, using dinitrobenzenes and copper (II) salts.[31] The dinitrobenzenes are

good electron acceptors, and would transform the radical ion (V) to (I), completely stopping C-alkylation by the radical pathway.[31]

$$ArCH_2Cl^{\bullet -} + A \rightarrow ArCH_2Cl + A^{\bullet -} \qquad (23)$$

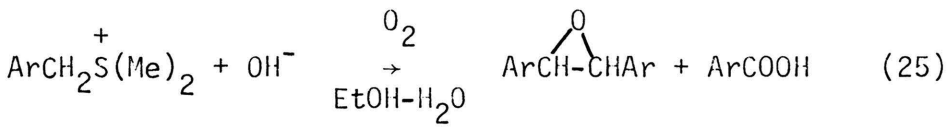
A = electron acceptor

Oxygen may act in a similar manner to give superoxide ion ($O_2^{\bullet -}$).[29] No detectable coupled product results in the presence of oxygen; instead, the 2-nitro-2-propyl anion is converted to acetone and nitrite ion (eq 24).[29]

$$CH_3\text{-}\overset{-}{\underset{NO_2}{C}}\text{-}CH_3 + \tfrac{1}{2}\, O_2 \rightarrow CH_3\overset{O}{\overset{\|}{C}}CH_3 + NO_2^- \qquad (24)$$

Although p-nitrobenzyl chloride is not consumed in the reaction (eq 24), 2-nitro-2-propyl anion is stable to oxygen in the absence of the halide.[29]

The reaction of p-nitrobenzyldimethylsulfonium bromide with sodium hydroxide in 50% aqueous ethanol has been investigated by Russell and Danen, to see if radical ions are involved in the formation of p,p'-dinitrostilbene.[29] The reaction was shown to be light-catalyzed; however, it proceeds at a satisfactory rate in the dark. Oxygen was shown to inhibit the formation of the stilbene (II); the products then are p,p'-dinitrostilbene oxide (68%), and p-nitrobenzoic acid (23%).[29]



$$ArCH_2\overset{+}{S}(Me)_2 + OH^- \xrightarrow[EtOH\text{-}H_2O]{O_2} ArCH\text{-}CHAr + ArCOOH \qquad (25)$$

No radical intermediates could be detected by ESR for the reaction of the sulfonium salt, presumably because of the low solubility of the stilbene (II) and its reduction products in aqueous solutions. The carbene mechanism could not be ruled out, and "may indeed be the correct mechanism."[29]

II. STATEMENT OF THE PROBLEM

It is evident from the foregoing historical introduction that the p-nitrobenzyl system is unusually reactive, particularly in basic media. The present work was undertaken primarily to distinguish between the paths represented by eq 8c and 8d, 8e, and to investigate the role, if any, of radical anions in stilbene formation.

$$ArCH_2Cl + OH^- \rightleftarrows Ar\dot{C}HCl + H_2O \qquad (8a)$$

$$ArCHCl \xrightarrow{rds} ArCH: + Cl^- \qquad (8b)$$

$$2\ ArCH: \rightarrow ArCH{=}CHAr \qquad (8c)$$

$$\underline{or}\ ArCH: + Ar\dot{C}HCl \rightarrow Ar\dot{C}HCHClAr \qquad (8d)$$

$$Ar\dot{C}HCHClAr \rightarrow ArCH{=}CHAr + Cl^- \qquad (8e)$$

The two paths, (eq 8c and 8d, 8e), although indistinguishable kinetically, can be tested by measuring the chlorine kinetic isotope effect. In pathway 8c, all of the chloride ion is lost in the rate-determining step, a process which should exhibit a large kinetic isotope effect.[32] The production of a very unstable intermediate such as a carbene or carbonium ion is expected to give a large kinetic isotope effect, because the C--Cl bond would be essentially broken in the transition state. For example, the first-order solvolysis of t-butyl chloride has a chlorine kinetic isotope effect k_{35}/k_{37} = 1.0106 at 20°C.[33] A similarly large effect is expected for path 8c. The pathway represented by eq 8d, 8e should

show a smaller effect, because only one-half of the chloride ion is expelled in the rate-determining step; the rest is lost in a subsequent fast step. The resultant kinetic isotope effect should be about one-half of that expected for equation 8c.

As the work progressed, it became evident that a reinvestigation of previously studied p-nitrobenzyl compounds, as well as the investigation of p-nitrobenzyl tosylate in basic media was necessary. The work that evolved will be presented in three main parts: (A) the reactions of p-nitrobenzyl chloride, (B) the reactions of p-nitrobenzyldimethylsulfonium salts, and (C) the reactions of p-nitrobenzyl tosylate, bromide, and iodide.

The first part, a study of the reactions of p-nitrobenzyl chloride, particularly its transformation to p,p'-dinitrostilbene, deals with the following topics: (1) deuterium exchange studies, (2) deuterium isotope effects, (3) chlorine kinetic isotope effects, (4) effect of light on the rate of reaction, (5) effect of oxygen on the rate and products, (6) effect of added dinitrobenzene on the rate and products, (7) ESR studies, and (8) the effect of di-t-butyl nitroxide on the rate and products. The exchange studies and deuterium isotope effects, employing α,α-d_2-p-nitrobenzyl chloride, were conducted to investigate earlier reports[9,34] concerning the extent and kinetics of the reversible carbanion formation. The chlorine kinetic isotope effect (3), k_{35}/k_{37}, was measured to determine the fate of the proposed carbene intermediate. The effect of illumination (4) on the rate of reaction was measured to evaluate the importance of radical anions in the production of p,p'-dinitrostilbene. The claim that the reaction of (I) with hydroxide ion

is not light-catalyzed (daylight vs dark) has been made.[17] Studies with p-nitrobenzyldimethylsulfonium bromide[29] suggest that a stronger source of illumination should be used to test the effect of light on the rate of the reaction. The products of the reaction of p-nitrobenzyl chloride in the presence and in the complete absence of oxygen (5) were studied, and the effect of oxygen on the rate of chloride ion liberation determined. The claim that oxygen does not alter the products of the p-nitrobenzyl chloride reaction[35] was tested, in light of the work of Russell and Danen. The effect of added electron acceptors (6) (m- and p-dinitrobenzenes)[28,31] on the kinetics and the products of the reaction were determined. ESR studies (7) were attempted to detect the possibility of radical intermediates. The effect of di-t-butyl nitroxide (8),[36*] an effective radical scavenger,[37] on the p-nitrobenzyl chloride--p,p'-dinitrostilbene transformation was investigated.

The second part of the work was the study of the reactions of p-nitrobenzyldimethylsulfonium tosylate (1) and bromide (2). The effect of added oxygen and di-t-butyl nitroxide was investigated to see if the sulfonium salts behaved in a similar manner as p-nitrobenzyl chloride.

The third part of the work was a study of three other p-nitrobenzyl compounds: p-nitrobenzyl tosylate, p-nitrobenzyl bromide, and p-nitrobenzyl iodide. The reaction of p-nitrobenzyl tosylate (1) is of interest because studies with 2-nitro-2-propyl

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*Small amounts of the nitroxide were effective in stopping a base-induced elimination; this was taken as proof that the reaction occurred by a radical chain process.

anion suggest that the tosylate is intermediate in behavior between p-nitrobenzyl chloride and p-nitrobenzyl bromide.[26] The change of products that occurs with the change of leaving group for certain reactions of p-nitrobenzyl compounds is difficult to explain, let alone predict. p-Nitrobenzyl tosylate could behave like p-nitrobenzyl chloride, giving the stilbene,[9] or undergo hydrolysis to give p-nitrobenzyl alcohol, or behave like p-nitrobenzyl bromide, giving p,p'-dinitrobibenzyl ether.[17] The behavior of the tosylate serves to assess the effect of a good leaving group on the production of p,p'-dinitrostilbene. The reactions of p-nitrobenzyl bromide and p-nitrobenzyl iodide (2) were re-examined for comparison purposes.

III. RESULTS AND DISCUSSION

A. Studies on p-Nitrobenzyl Chloride

1. Exchange Studies. The exchange of the side-chain protons of p-nitrobenzyl chloride was studied using α,α-d_2-p-nitrobenzyl chloride. The extent of deuteration was determined using the ratio of the NMR signals of the benzylic protons to the aromatic protons. Unreacted p-nitrobenzyl chloride, from the reaction mixture of 0.10 M NaOH and 0.01 M α,α-d_2-p-nitrobenzyl chloride in 50% aqueous dioxane at 25°C, was recovered after 42% reaction. NMR analysis showed a ratio of aromatic protons to benzylic protons, of 8 : 1, equivalent to an equimolar mixture of α-d-p-nitrobenzyl chloride and α,α-d_2-p-nitrobenzyl chloride. Therefore, one-half of the recovered p-nitrobenzyl chloride had been reprotonated. The extent of the exchange, 50% after 42% reaction is essentially the same as the value previously reported, 42% exchange after 38% reaction.[9*] The latter value for the exchange was obtained from the reaction of p-nitrobenzyl chloride in 80% dioxane--20% D_2O.[9]

A similar exchange study was undertaken for the reaction of p-nitrobenzyl chloride in the presence of p-nitrobenzaldehyde; the products in this case are cis- and trans-p,p'-dinitrostilbene oxides (eq 5).[6,9] Unreacted p-nitrobenzyl chloride recovered from

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*The amount of deuteration in the recovered p-nitrobenzyl chloride was calculated by comparison of the ratio of the height of the absorption bands at 12.7 μ and 6.1 μ in the infrared, to the ratio in a sample considered to be 66% deuterated.[9] This standard sample, prepared by chlorination of mono-deuterated toluene, would be expected to consist of 2/3 α-d-p-nitrobenzyl chloride and 1/3 p-nitrobenzyl chloride; this is really 33% deuterated in the benzylic position. Therefore, the 42% deuteration reported in the recovered p-nitrobenzyl chloride was actually 21%.

the reaction of 0.01 M α,α-d_2-p-nitrobenzyl chloride, 0.01 M p-nitrobenzaldehyde, and 0.10 M NaOH in 50% aqueous dioxane at 25°C, showed no exchange after 50% reaction. This is completely consistent with results reported previously.[17] Thus, the aldehyde successfully intercepts essentially every carbanion in a rapid step, and the carbanion formation is rate-determining.[17]

The magnitude of the exchange during the p-nitrobenzyl chloride--p,p'-dinitrostilbene transformation is the basis of several kinetic arguments in the literature.[9,17,34] An alkylation-dehydrohalogenation mechanism[9] and a mechanism involving radicals[17] for this transformation have been ruled out on the basis of these kinetic arguments. The magnitude of the exchange is also not consistent with arguments that compare the rate of the reverse step of the equilibrium (eq 8a) with the rate of α-elimination (eq 8b), giving the proposed p-nitrophenyl carbene.[34] Starting with the mechanism proposed for the production of p,p'-dinitrostilbene (eq 26), the overall rate constant in terms of the basic steps for the rate expression (eq 27) may be obtained from the steady state approximation.

$$ArCH_2Cl + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} Ar\dot{C}HCl^- + H_2O \qquad (26a)$$

$$Ar\dot{C}HCl^- \xrightarrow{k_2} ArCH: + Cl^- \qquad (26b)$$

$$2\ ArCH: \xrightarrow{k_3} ArCH{=}CHAr \qquad (26c)$$

<u>or</u>

$$ArCH: + Ar\bar{C}HCl \xrightarrow{k_4} ArCH{=}CHAr + Cl^- \quad (26d)$$

$$Rate = k' [ArCH_2Cl]\cdot[OH^-] \quad (27)$$

If we first consider the pathway in which two carbenes dimerize (eq 26a, b, c), we may write the following expressions.

$$Rate = -d[ArCH_2Cl]/dt = +d[Cl]/dt \quad (28)$$

$$-d[Ar\bar{C}HCl]/dt = k_{-1}[Ar\bar{C}HCl]\cdot[H_2O] + k_2[Ar\bar{C}HCl] - k_1[ArCH_2Cl]\cdot[OH^-] \quad (29)$$

If one assumes that all steps after the elimination step (eq 26b) are rapid, and that the forward part of the equilibrium (eq 26a) proceeds at a faster rate than the elimination step, then the steady state approximation is valid.

$$d[Ar\bar{C}HCl]/dt = 0 \quad \text{(steady state approximation)} \quad (30)$$

Solving equation 29 for the concentration of the carbanion, one obtains:

$$[Ar\bar{C}HCl] = \frac{k_1[ArCH_2Cl]\cdot[OH^-]}{k_{-1}[H_2O] + k_2} \quad (31)$$

<u>and</u>

$$Rate = k_2[Ar\bar{C}HCl] \quad (32)$$

<u>or</u>

$$Rate = \frac{k_1k_2[ArCH_2Cl]\cdot[OH^-]}{k_{-1}[H_2O] + k_2} \quad (33)$$

From eq 27, it is seen that the overall rate constant for this pathway (eq 26a, b, c) is:

$$k' = \frac{k_1 k_2}{k_{-1}[H_2O] + k_2} \tag{34}$$

For the other pathway (eq 26a, b, d), in which the carbene reacts with a carbanion, the same treatment is applicable; however, because a second carbanion is consumed in a fast step (eq 26d) following the rate-determining step, the overall picture is slightly different.

$$\text{Rate} = -d[ArCH_2Cl]/dt = +d[Cl]/dt \tag{35}$$

$$-d[Ar\bar{C}HCl]/dt = k_{-1}[Ar\bar{C}HCl]\cdot[H_2O] + k_2[Ar\bar{C}HCl] - k_1[ArCH_2Cl]\cdot[OH^-] + k_4[ArCH:]\cdot[Ar\bar{C}HCl] \tag{36}$$

$$-d[ArCH:]/dt = k_4[ArCH:]\cdot[Ar\bar{C}HCl] - k_2[Ar\bar{C}HCl] \tag{37}$$

Making the same assumptions as in the first case, we may apply the steady state approximation to eqs 36 and 37. Substituting eq 37 into eq 36, one obtains the concentration of the carbanion (eq 38).

$$[Ar\bar{C}HCl] = \frac{k_1[ArCH_2Cl]\cdot[OH^-]}{k_{-1}[H_2O] + 2\,k_2} \tag{38}$$

The rate of the reaction is equal to the rate of release of chloride ion; this is twice the rate of the second step (26b), because every carbene reacts with a carbanion releasing the second chloride ion.

$$\text{Rate} = 2\ k_2[\text{ArCHCl}^-] \tag{39}$$

or

$$\text{Rate} = \frac{2\ k_1 k_2[\text{ArCH}_2\text{Cl}]\cdot[\text{OH}^-]}{k_{-1}[\text{H}_2\text{O}] + 2\ k_2} \tag{40}$$

Therefore, the overall rate constant, k', for this pathway (eq 26a, b, d) is given by:

$$k' = \frac{2\ k_1 k_2}{k_{-1}[\text{H}_2\text{O}] + 2\ k_2} \tag{41}$$

Equation 34 has been given as the overall rate constant for both pathways;[34] it is valid only for the pathway in which two carbenes dimerize (eq 26c).

Equation 34 has been used to obtain the ratio of the relative number of carbanions that are reprotonated to those that undergo an α-elimination, giving the proposed p-nitrophenyl carbene.[34] A good approximate value for the forward part of the equilibrium (eq 26a) is given by the rate expression for the reaction of p-nitrobenzyl chloride and hydroxide ion in the presence of p-nitrobenzaldehyde;[34] in this case, the proton abstraction is rate-determining.[17,34]

$$\text{Rate} = k_1[\text{ArCH}_2\text{Cl}]\cdot[\text{OH}^-] \tag{42}$$

With the same concentrations of base and p-nitrobenzyl chloride, the reaction with added p-nitrobenzaldehyde, giving p,p'-dinitrostilbene oxides, is approximately three times faster than the corresponding

reaction of p-nitrobenzyl chloride and hydroxide ion alone.[9] From the relative rates of these two reactions (eq 43), and substituting the value of k' from equation 34 into equation 27, one obtains the ratio of carbanions that have been exchanged to those that have undergone α-elimination for the case of carbene dimerization (eq 26c).

$$\text{Rate}_{(\text{eq } 42)} \cong 3\ \text{Rate}_{(\text{eq } 27)} \tag{43}$$

$$k_1[ArCH_2Cl]\cdot[OH^-] \cong 3\{k_1k_2/k_{-1}[H_2O] + k_2)\}\cdot[ArCH_2Cl]\cdot[OH^-] \tag{44}$$

By elimination of terms, and rearranging, the ratio is obtained.

$$\frac{k_{-1}[H_2O]}{k_2} \cong 2 \tag{44}$$

However, for the case of reaction of the carbene with a carbanion (eq 26d), the expression becomes:

$$k_1[ArCH_2Cl]\cdot[OH^-] \cong 3\{2k_1k_2/(k_{-1}[H_2O] + 2k_2)\}\cdot[ArCH_2Cl]\cdot[OH^-] \tag{45}$$

This is reduced to the ratio:

$$\frac{k_{-1}[H_2O]}{k_2} \cong 4 \tag{46}$$

Equation 44 has been incorrectly given as the rate constant for both pathways.[34]

The ratios obtained (eq 44 and 46) may be easily tested by using the value of the exchange that we have measured. Let us first consider the pathway in which two carbenes dimerize (eq 26c). For

every 100 molecules of p-nitrobenzyl chloride initially present, after 42% reaction, 58 molecules would remain; because these were 50% exchanged, 29 carbanions would have been reprotonated. In this pathway, all of the carbanions that were converted to the product would have undergone an α-elimination; therefore 42 carbanions were involved in the rate-determining step (eq 26b). The ratio in equation 44 would be:

$$\frac{k_{-1}[H_2O]}{k_2} = \frac{29}{42} \qquad \underline{or} \qquad \frac{k_{-1}[H_2O]}{k_2} \cong 0.7 \tag{47}$$

This is a very poor approximation of the ratio predicted by equation 44. Using the previously reported value of the exchange,[9] the expression is almost identical:

$$\frac{k_{-1}[H_2O]}{k_2} = \frac{26}{38} \qquad \underline{or} \qquad \frac{k_{-1}[H_2O]}{k_2} \cong 0.7 \tag{48}$$

For the second pathway (eq 26d), the number of carbanions that have been exchanged would be the same. However, of the 42 carbanions that have been converted to products, only 21 would have undergone an α-elimination; the rest would have reacted with a carbene in a fast step (eq 26d) following the rate-determining step. Therefore, the ratio would be:

$$\frac{k_{-1}[H_2O]}{k_2} = \frac{29}{31} \qquad \underline{or} \qquad \frac{k_{-1}[H_2O]}{k_2} \cong 1.4 \tag{49}$$

Therefore, the size of the exchange is too small to be consistent with the kinetic arguments of Dolieb and Iskander.[34]

The possibility of an aklylation-dehydrohalogenation mechanism (eq 50) must be considered. For such a mechanism, one would expect complex kinetics.

$$ArCH_2Cl + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} Ar\bar{C}HCl + H_2O \qquad (50a)$$

$$Ar\bar{C}HCl + ArCH_2Cl \xrightarrow{k_2} ArCH_2CHClAr + Cl^- \qquad (50b)$$

$$ArCH_2CHClAr + OH^- \xrightarrow{k_3} ArCH{=}CHAr + Cl^- + H_2O \qquad (50c)$$

$$2\ ArCH_2Cl + 2\ OH^- \rightarrow ArCH{=}CHAr + 2\ H_2O + 2\ Cl^- \qquad (50d)$$

If one assumes that all steps after the second step (eq 50b) are rapid, and that the forward part of the equilibrium (eq 50a) proceeds at a faster rate than the alkylation step (eq 50b), then one may write:

$$\text{Rate} = -d[ArCH_2Cl]/dt = +d[Cl]/dt \qquad (51)$$

$$d[Ar\bar{C}HCl]/dt = k_1[ArCH_2Cl]\cdot[OH^-] - k_{-1}[Ar\bar{C}HCl]\cdot[H_2O] - k_2[ArCH_2Cl]\cdot[Ar\bar{C}HCl] \qquad (52)$$

$$d[Ar\bar{C}HCl]/dt = 0 \quad \text{(steady state approximation)} \qquad (53)$$

$$[Ar\bar{C}HCl] = k_1[ArCH_2Cl]\cdot[OH^-]/(k_{-1}[H_2O] + k_2[ArCH_2Cl]) \qquad (54)$$

By substitution of the concentration of the carbanion into the rate expression (eq 55), we obtain:

$$\text{Rate} = 2\ k_2[\text{ArCHCl}^-]\cdot[\text{ArCH}_2\text{Cl}] \tag{55}$$

$$\text{Rate} = 2\ k_1k_2[\text{ArCH}_2\text{Cl}]^2\cdot[\text{OH}^-] \,/\, (k_{-1}[\text{H}_2\text{O}] + k_2[\text{ArCH}_2\text{Cl}]) \tag{56}$$

Because the concentration of water is essentially constant, the expression may be rewritten as:

$$\text{Rate} = \frac{k'[\text{ArCH}_2\text{Cl}]^2\cdot[\text{OH}^-]}{k'' + k_2[\text{ArCH}_2\text{Cl}]} \tag{57}$$

where $k' = 2\ k_1k_2$

and $k'' = k_{-1}[\text{H}_2\text{O}]$

In this general form, it can be seen that the kinetics are complex, and that the rate expression cannot be written in the simple form:

$$\text{Rate} = k[\text{ArCH}_2\text{Cl}]^n\cdot[\text{OH}^-] \tag{58}$$

However, if the first term in the denominator of equation 57 is very much larger than the second term ($k'' \gg k_2[\text{ArCH}_2\text{Cl}]$), then the second term may be neglected, and the rate expression would be reduced to a simple form (eq 59).

$$\text{Rate} = \frac{k'[\text{ArCH}_2\text{Cl}]^2\cdot[\text{OH}^-]}{k''} = k_{exp}[\text{ArCH}_2\text{Cl}]^2\cdot[\text{OH}^-] \tag{59}$$

This equation would be valid for the case in which the reverse step

of the equilibrium is much faster than the alkylation step; the reaction would show a large D-exchange.

If $k_2[ArCH_2Cl] >> k''$, as would be reflected in a small rate of exchange, one would observe second order kinetics (eq 60).

$$\text{Rate} = \frac{k'[ArCH_2Cl]^2 \cdot [OH^-]}{k_2[ArCH_2Cl]} = k_{exp}[ArCH_2Cl] \cdot [OH^-] \qquad (60)$$

For intermediate cases, the kinetics would still be complicated, showing a change in apparent order with time. If, for example, the two terms in the denominator (eq 57) were equal at the start of the reaction, then for initial points, $k'' = k_2[ArCH_2Cl]$, and the rate would obey the following expression:

$$\text{Rate} = \frac{k'[ArCH_2Cl]^2 \cdot [OH^-]}{2\ k_1[ArCH_2Cl]} \qquad (61)$$

This is just eq 60 in slightly different form. However, as the reaction progresses, the two terms in the denominator will no longer be equal, and one should observe a deviation from second-order kinetics.

It suffices to say that an alkylation-dehydrohalogenation mechanism cannot be ruled out on the assumption that it will always show third-order kinetics.[9]

The following radical anion mechanism has been ruled out, based on kinetic arguments.[17] However, the same considerations that apply to the alkylation-dehydrohalogenation mechanism could also be applied

to this mechanism. Such a mechanism (eq 62) could show either second or third-order kinetics, depending on the rate of exchange.

$$ArCH_2Cl + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} Ar\bar{C}HCl + H_2O \qquad (62a)$$

$$Ar\bar{C}HCl + ArCH_2Cl \xrightarrow[h\nu]{k_2} Ar\dot{C}HCl + ArCH_2Cl^{\bullet -} \qquad (62b)$$

$$ArCH_2Cl^{\bullet -} \xrightarrow{k_3} ArCH_2\bullet + Cl^- \qquad (62c)$$

$$ArCH_2\bullet + Ar\dot{C}HCl \xrightarrow{k_4} ArCH_2CHClAr \qquad (62d)$$

$$ArCH_2CHClAr + OH^- \xrightarrow{k_5} ArCH{=}CHAr + Cl^- + H_2O \qquad (62e)$$

If the second step (eq 62b) is rate-determining, then this mechanism would show the same kinetics as that of the alkylation-dehydrohalogenation mechanism, and likewise cannot be dismissed.

2. Deuterium Isotope Effects. The kinetic isotope effect, k_H/k_D, was measured for the reaction of α,α-d_2-p-dinitrobenzyl chloride and hydroxide ion in 50% aqueous at 25°C; the data are given in Tables II and III. The unlabeled compound was prepared by the same procedure as the labeled p-nitrobenzyl chloride.

The kinetic isotope effect, k_H/k_D, was obtained from the average rate constants of the two kinetic runs. The average of the points for one half-life was used in each case. The value of the isotope effect,

Table II

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane at 25°C, Run 71

0.01 M p-Nitrobenzyl Chloride

0.10 M NaOH

Time (sec)	1200	2400	3600	7200	10800	19800	25200
Reaction (%)	11.7	22.0	31.0	50.6	63.5	82.2	86.1
$k_2 \times 10^4$	10.47	10.44	10.48	10.07	9.65	9.20	8.27
(M^{-1} sec^{-1})	$\bar{k} = 10.37 \times 10^{-4}$ (for first 4 points)						

Table III

Reaction of α,α-d_2-p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane at 25°C, Run 72

0.01 M α,α-d_2-p-Nitrobenzyl Chloride

0.10 M NaOH

Time (sec)	1200	2400	3600	7200	10800	19800	25200
Reaction (%)	2.6	5.9	7.2	13.0	19.3	33.8	43.3
$k_2 \times 10^4$	2.18	2.53	2.09	1.94	2.00	2.12	2.30
(M^{-1} sec^{-1})	$\bar{k} = 2.16 \times 10^{-4}$ (all points)						

k_H/k_D = 4.80, is too large to be a secondary isotope effect. This is not obvious from the value published previously,[9] where the side chain was only partially deuterated (33% statistically),[9] and the isotope effect was accordingly diluted.

In a similar experiment, the deuterium kinetic isotope effect was determined for the reaction of α,α-d_2-p-nitrobenzyl chloride and hydroxide ion in the presence of p-nitrobenzaldehyde; the products in this case are cis- and trans-p,p'-dinitrostilbene oxides. The rate of reaction for this case is approximately three times faster than for the reaction of p-nitrobenzyl chloride and hydroxide ion alone. The deuterium kinetic isotope effect obtained in this case, k_H/k_D = 6.34, is significantly larger than the value obtained for the reaction of p-nitrobenzyl chloride giving p,p'-dinitrostilbene. Calculations based on the difference in zero-point energy predict a factor of 7 in the rate for the breaking of C--H vs C--D bonds.[38] Because no exchange is occurring in this case, the isotope effect obtained is a true measure of the relative rate of carbanion formation for the unlabeled vs the labeled compound.

The deuterium isotope effect was also determined for a case with partial deuteration of the side chain (Tables VI and VII).

The apparent isotope effect obtained in this case, k_H/k_D = 1.60, is evidently diluted; the hydrogen, rather than deuterium, is preferentially abstracted during carbanion formation.

The large primary kinetic isotope effect, k_H/k_D = 4.80, confirms that the exchange of the α-protons is not occurring rapidly in comparison to the steps leading to the products. If the exchange

Table IV

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion with added p-Nitrobenzaldehyde in 50% Aqueous Dioxane at 25°C, Run 73

0.01 M p-Nitrobenzyl Chloride

0.01 M p-Nitrobenzaldehyde

0.10 M NaOH

Time (sec)	1200	2400	3600	4800	6000
Reaction (%)	35.4	56.6	69.5	78.6	82.5
$k_2 \times 10^3$	3.72	3.58	3.46	3.37	3.06
(M^{-1} sec^{-1})			$\bar{k} = 3.43 \times 10^{-3}$		

Table V

Reaction of α,α-d_2-p-Nitrobenzyl Chloride and Hydroxide Ion with added p-Nitrobenzaldehyde in 50% Aqueous Dioxane at 25°C, Run 74

0.01 M α,α-d_2-p-Nitrobenzyl Chloride

0.01 M p-Nitrobenzaldehyde

0.10 M NaOH

Time (sec)	1200	2400	3600	4800	6000	7200	10800
Reaction (%)	6.3	12.9	17.9	23.4	27.5	31.2	42.1
$k_2 \times 10^4$	5.42	5.78	5.54	5.62	5.44	5.26	5.17
(M^{-1} sec^{-1})				$\bar{k} = 5.41 \times 10^{-4}$			

Table VI

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane at 25°C, Run 69

0.05 M p-Nitrobenzyl Chloride

0.05 M NaOH

Time (sec)	1200	2400	3600	4800	7200	18000	27200
Reaction (%)	6.4	11.3	15.0	18.2	25.6	40.3	52.5
$k_2 \times 10^4$	11.29	10.65	9.82	9.29	9.55	7.49	8.14
(M^{-1} sec^{-1})			$\bar{k} = 9.46 \times 10^{-4}$				

Table VII

Reaction of α-$\underline{d}_1$-p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane at 25°C, Run 70

0.05 M α-$\underline{d}_1$-p-Nitrobenzyl Chloride

0.05 M NaOH

Time (sec)	1200	2500	3600	5060	6000	7500
Reaction (%)	4.5	7.6	9.9	12.1	13.8	17.6
$k_2 \times 10^4$	7.87	6.60	6.10	5.44	5.32	5.70
(M^{-1} sec^{-1})						

Time (sec)	12600	21600	30600
Reaction (%)	21.7	35.3	48.0
$k_2 \times 10^4$	4.96	5.05	6.02
(M^{-1} sec^{-1})		$\bar{k} = 5.90 \times 10^{-4}$	

were very rapid, the labeled atoms on the side chain would be lost, resulting in a distinctly smaller kinetic isotope effect. The primary kinetic isotope effect confirms that proton abstraction, giving the carbanion, proceeds or is concurrent with the rate-determining step.

Comparison of the kinetic isotope effect for the reaction of p-nitrobenzyl chloride, $k_H/k_D = 4.80$, with that for the reaction with added p-nitrobenzaldehyde, $k_H/k_D = 6.34$, shows that the isotope effect in the first case is diluted. Because the rate expressions are the same in the two cases, one would have expected similar isotope effects. However, in the case of formation of p,p'-dinitrostilbene, the carbanion formation is a part of an equilibrium; with added p-nitrobenzaldehyde, the reverse step does not occur. The exchange that occurs because of the equilibrium could cause a dilution of the isotope effect by a gradual substitution of protons for deuterons; this would be accompanied by a gradual increase of rate constants with time. This does not seem to be the case (see Figure 1). Another possibility would be the intervention of side reactions which could dilute the kinetic isotope effect.

3. Chlorine kinetic isotope effects. Bonds with a light isotope are broken more readily than those with the heavy isotope. Therefore, if a compound with C--Cl bonds is allowed to undergo a reaction in which those bonds are broken in a rate-determining step, the isotopic abundance of that compound will change with time. If recovered p-nitrobenzyl chloride from its reaction with hydroxide ion is examined, it will show a greater content of Cl^{37} than the

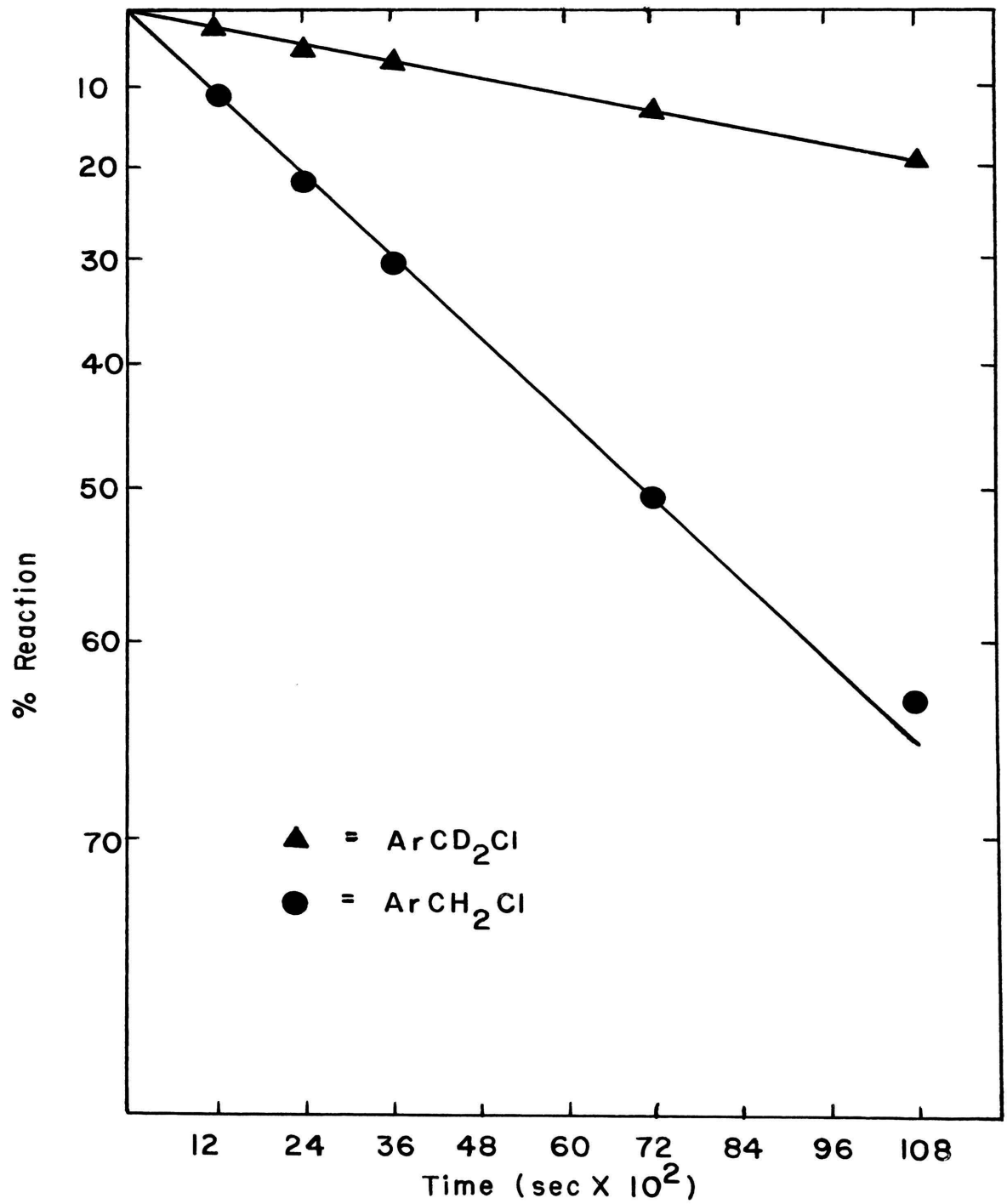

Figure 1. Plot of log % reaction vs time for reaction of 0.01 M p-nitrobenzyl chloride and 0.10 M sodium hydroxide in 50% aqueous dioxane at 25°C

original material if the C--Cl bond is broken at or before the transition state. Furthermore, the ionic chloride released will show a corresponding enrichment in the lighter isotope. We can designate the original abundance of the two isotopes of chlorine as (R_{37}/R_{35}), where R stands for the chlorine in the reactant. This ratio is obtained from the complete reaction of p-nitrobenzyl chloride. The abundance of the chloride ion from a reaction quenched after only a few percent reaction is designated as the product sample, (P_{37}/P_{35}). These values may be measured directly on a double collector mass spectrometer. The samples are introduced as a gaseous methyl chloride. The chlorine kinetic isotope effect is given by the formula:

$$k_{35}/k_{37} = \frac{(R_{37}/R_{35})}{(P_{37}/P_{35})} \qquad (63)$$

The validity of eq 63 is discussed in Appendix A.

The conversion of the ionic chloride to methyl chloride has been worked out by Hill and Fry.[3] A special procedure for the precipitation of the silver chloride used for that conversion is given by Taylor and Grimsrud.[39]

The value obtained for the reaction of 0.01 M p-nitrobenzyl chloride and 0.10 M NaOH in 50% aqueous dioxane at 25°C, was 1.0041 ± 0.0004. This value is about one-half of the value found by Hill and Fry for S_N1 reactions of various substituted benzyl halides; they found an average value of 1.0078 for S_N1 processes,

and 1.0058 for S_N2 processes.[3] It is reasoned that the breaking of a C--Cl bond to give a divalent intermediate would give a large kinetic isotope effect, like that for an S_N1 process.

$$ArCHCl \rightarrow ArCH: + Cl^- \qquad (64)$$

For such an α-elimination, leading to a very unstable intermediate, the transition state should resemble the carbene much more closely than the carbanion. The C--Cl bond would be extensively ruptured in the transition state. This would be a case similar to the formation of a carbonium ion; for the formation of an unstable intermediate. The chlorine kinetic isotope effect for the solvolysis of t-butyl chloride is 1.0106;[33] the solvolysis is a pure S_N1 process.

The value that we measured for p-nitrobenzyl chloride is about one-half of the value that we expect for the loss of all the chloride ions in the rate-determining step. Therefore, we conclude that only one of two C--Cl bonds is broken in the slow step, followed by loss of a second chloride ion in a rapid, indiscriminate step. This is consistent with the steps represented by eq 8d and 8e, but not by eq 8c. It is also consistent with the alkylation-dehydrohalogenation mechanism (eq 50a, b, c).

4. Effect of Light. A 140 watt Hanovia lamp at a distance of 6 inches was used as the source of illumination. The rates of reaction of p-nitrobenzyl chloride in the dark, and with illumination are given in Tables VIII and IX.

The kinetics indicate that the reaction is slightly light catalyzed, contrary to the previous report.[17] Although the reaction

Table VIII

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane at 25°C, Run 61

0.01 M p-Nitrobenzyl Chloride

0.10 M NaOH

Opaque Flask

Time (sec)	1200	2400	3600	4800	6000
Reaction (%)	11.3	22.6	28.2	37.8	43.1
$k_2 \times 10^4$ (M^{-1} sec^{-1})	9.67	10.70	9.25	8.60	9.60
			$\bar{k} = 9.56 \times 10^{-4}$		

Table IX

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane at 25°C, Run 60

0.01 M p-Nitrobenzyl Chloride

0.10 M NaOH

Ordinary Flask

Time (sec)	1200	2400	3600	4800	6000
Reaction (%)	12.9	25.2	33.4	42.3	49.2
$k_2 \times 10^4$ (M^{-1} sec^{-1})	11.32	12.11	11.47	11.71	11.59
			$\bar{k} = 11.64 \times 10^{-4}$		

proceeds at a satisfactory rate in total darkness, the illumination caused a rate increase of about 20%, which is too large to be ignored. The increase in the rate is much smaller than that observed for the reaction of p-nitrobenzyldimethylsulfonium bromide, using a 275 watt GE sunlamp.[29] This is probably due to the greater portion of energy transmitted in the region above 3000 Å in the latter case.

The increased rate is suggestive of a radical mechanism;[29] however light has been shown to accelerate the decomposition of certain ylides, giving the corresponding carbenes.[40] Therefore, the faster rate might also be explained in terms of an α-elimination, giving p-nitrophenyl carbene.

$$ArCHCl^- \xrightarrow{h\nu} ArCH: + Cl^- \qquad (65)$$

Although a divalent intermediate cannot be ruled out, a radical anion intermediate should also be considered. The alkylation of 2-nitro-2-propyl anion by p-nitrobenzyl chloride in ethanol presumably occurs by a radical chain process in which p-nitrobenzyl chloride radical anion is an intermediate; the chain process occurs only with illumination.[29] The same reaction, in DMF, occurs without illumination, but at a slower rate.[28,29] Other examples of light-induced formation of radical anions are afforded by THF solutions of nitrobenzene,[41*] and also tetracyanoethylene (TCNE);[42] in both cases, an ESR signal is detected with irradiation. In the latter case, the TCNE radical anion is observed with only ordinary room light, but

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*Irradiation causes the nitro group to abstract an α-hydrogen from THF.

not in total darkness.[42] Light facilitates electron transfer, thereby generating radicals; small traces of impurities may start a radical chain.[43*]

A scheme similar to that for C-alkylation (eq 18-21), could explain the formation of p,p'-dinitrostilbene.

$$\underset{\text{(I)}}{ArCH_2Cl} + OH^- \rightleftarrows Ar\bar{C}HCl + H_2O \qquad (66a)$$

$$(I) + e^- \rightarrow \underset{\text{(V)}}{ArCH_2Cl^{\bullet -}} \qquad (66b)$$

$$(V) \rightarrow \underset{\text{(VI)}}{ArCH_2^{\bullet}} + Cl^- \qquad (66c)$$

$$(VI) + Ar\bar{C}HCl \rightarrow ArCH_2CHClAr^{\bullet -} \qquad (66d)$$

$$ArCH_2CHClAr^{\bullet -} + OH^- \rightarrow ArCH{=}CHAr^{\bullet -} + H_2O + Cl^- \qquad (66e)$$

$$ArCH{=}CHAr^{\bullet -} + (I) \rightarrow \underset{\text{(II)}}{ArCH{=}CHAr} + (V) \qquad (66f)$$

<u>or</u> $$ArCH_2CHClAr^{\bullet -} + (I) \rightarrow ArCH_2CHClAr + (V) \qquad (66g)$$

<u>and</u> $$ArCH_2CHClAr + OH^- \rightarrow (II) + H_2O + Cl^- \qquad (66h)$$

A possible non-chain process would involve the transfer of one electron from the carbanion of p-nitrobenzyl chloride to a neutral

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*An example is: $[Fe^{+++}(OH)^-]^{++} \xrightarrow{h\nu} Fe^{++} + \cdot OH$

molecule, giving a radical and a radical anion (eq 62a-e).[17] An analogous mechanism was considered for the dimerization of p-nitrotoluene in strong base, giving p,p'-dinitrobibenzyl.[44]

In both schemes, eq 66 and 62, the critical intermediate is the p-nitrobenzyl chloride radical anion (V). Due to its instability,[45,46] it would be very difficult to detect during the (I) → (II) transformation. However, an ESR signal attributed to the radical anion (V) has been reported in basic solutions of (I) in ethanol--water, by workers using a flow technique.[47] Water is added to dipolar aprotic solvents to stabilize highly reactive halogenated nitroaromatic anion radicals, by retarding anion expulsion.[48]

5. Effect of oxygen. Iskander and Riad state that "... the presence of both oxygen and p-nitrobenzyl alcohol (or even t-butyl alcohol) is necessary for the formation of cis- and trans-p,p'-dinitrostilbene oxides by the action of alkali on p-nitrobenzyl chloride in 50% aqueous dioxane, while in the absence of any of these two reagents the epoxides are not formed, but p,p'-dinitrostilbene is the only product."[35] However, in our initial experiments with p-nitrobenzyl chloride, we have observed two spots with R_f values identical to those of cis- and trans-p,p'-dinitrostilbene oxides, as well as several other minor unidentified spots. Therefore, we determined the effect of saturating the medium with oxygen on the reaction of p-nitrobenzyl chloride (Table X).

No traces of p,p'-dinitrostilbene could be detected by tlc; the precipitate was exclusively cis- and trans-p,p'-dinitrostilbene

Table X

Reaction Products of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane Saturated with Oxygen

0.02 M p-Nitrobenzyl Chloride

0.10 M NaOH

Reaction time: 24 hr

Compound	% Yield
cis-p,p'-dinitrostilbene oxide	51.0
trans-p,p'-dinitrostilbene oxide	37.0
p-nitrobenzyl alcohol	5.2
p-nitrobenzoic acid	4.0
p-nitrobenzaldehyde	2.0

oxides, and had only slight traces of impurities. By contrast, the product which precipitates from the reaction of equimolar amounts of p-nitrobenzyl chloride and p-nitrobenzaldehyde with hydroxide ion in 50% aqueous dioxane contains small amounts of p,p'-dinitrostilbene and other compounds. Thus oxygen is completely effective in preventing the formation of the stilbene.

It is not possible to tell by the products alone, if oxygen prevents the formation of the stilbene by reacting with the carbanion, a radical intermediate, or a divalent intermediate. A study of the kinetics with an oxygen atmosphere, however, shows that the rate of reaction, as monitored by chloride titration, is slower by about 25% in the presence of excess oxygen (Tables XI and XII).

Table XI

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane Saturated with Oxygen at 25°C, Run 92

0.01 M p-Nitrobenzyl Chloride

0.26 M NaOH

Time (sec)	1200	2400	3700	5400	7500	9600
Reaction (%)	19.0	37.7	51.8	64.1	72.4	80.1
$k_2 \times 10^4$	6.73	7.62	7.70	7.41	6.70	6.60
(M^{-1} sec^{-1})			$\bar{k} = 7.13 \times 10^{-4}$			

Table XII

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane (Ordinary Solution) at 25°C, Run 93

0.01 M p-Nitrobenzyl Chloride

0.26 M NaOH

Time (sec)	1200	2400	3700	5400	7500	9600
Reaction (%)	27.3	48.9	62.1	72.5	78.2	84.9
$k_2 \times 10^4$	10.25	10.87	10.20	9.60	7.97	7.73
(M^{-1} sec^{-1})			$\bar{k} = 9.44 \times 10^{-4}$			

To determine if the p,p'-dinitrostilbene oxides are formed in the complete absence of oxygen, the reaction was repeated using degassed solutions. The precipitate obtained had a weight that was 98% of that expected for a quantitative yield of p,p'-dinitrostilbene; however, tlc and its visible and ultraviolet spectra showed that it contained the isomers of both p,p'-dinitrostilbene and p,p'-dinitrostilbene oxides, as well as smaller amounts of other compounds (Table XIII).

Table XIII

Reaction Products of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane (Solutions Degassed by 5 Freeze-Thaw cycles on a Vacuum Line Before Mixing)

Compound	% Yield
cis-p,p'-dinitrostilbene	27.8
trans-p,p'-dinitrostilbene	24.2
cis-p,p'-dinitrostilbene oxide	24.4
trans-p,p'-dinitrostilbene oxide	18.5
p-nitrobenzyl alcohol	3.2
p-nitrobenzaldehyde	0.1
p-nitrotoluene	trace
p,p'-dinitrotolane*	--

*observed by tlc, but amount not determined

The stilbene oxides formed in this case could not come from dissolved oxygen; therefore, the oxygen in the epoxide linkage probably comes from water (or hydroxide ion). The dioxane was carefully purified to remove peroxides which might cause a side reactions leading to stilbene oxides.

p-Nitrobenzaldehyde is presumed to be an intermediate in the production of the stilbene oxides. It was present in moderate concentrations during the reaction of p-nitrobenzyl chloride in the presence of oxygen (Table X). Analogously, electrolysis of DMF solutions of p-nitrobenzyl chloride gave an ESR signal for the radical anion of p-nitrobenzaldehyde, rather than that of p-nitrobenzyl chloride.[49*] The observed ESR signal was quantitative as long as the oxygen concentration was as high as that of the halide. It was proposed that p-nitrobenzyl radical (VI) reacts with oxygen to give rise to p-nitrobenzaldehyde.[49]

$$\underset{(I)}{ArCH_2Cl} + e^- \rightarrow \underset{(V)}{ArCH_2Cl^{\bullet -}} \qquad (67a)$$

$$ArCH_2Cl^{\bullet -} \rightarrow \underset{(VI)}{ArCH_2\bullet} + Cl^- \qquad (67b)$$

$$ArCH_2\bullet + O_2 + 2e^- \rightarrow ArCHO^{\bullet -} + OH^- \qquad (67c)$$

In our system, if (V) and (VI) are intermediates leading to the dinitrostilbene (II), oxygen could block the formation of (II) by intercepting (VI).

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*The same ESR signal was observed for a DMF solution of p,p'-dinitrobibenzyl; this suggests $ArCH_2\bullet$ as the intermediate.

Another possibility is that oxygen reacts with the carbanion of (I), giving a hydroperoxide intermediate. Hydroperoxide anions (ROO^-) or hydroperoxides (ROOH) are invariably invoked as intermediates in anion oxidations, but the products are seldom the hydroperoxides.[50,51*] If the oxidation of p-nitrobenzyl chloride gave p-nitrobenzaldehyde, then it would be rapidly converted to the stilbene oxides.[9] An analogy to the production of p-nitrobenzaldehyde from p-nitrobenzyl chloride is the oxidation of 2-nitropropane in weakly basic solutions by molecular oxygen.[52]

$$Me_2CHNO_2 + OH^- + \tfrac{1}{2} O_2 \rightarrow Me_2C{=}O + H_2O + NO_2^- \qquad (68)$$

In light of the mechanism for oxidation of 2-nitropropane, we propose the following steps for the p-nitrobenzyl chloride case.

$$ArCH_2Cl + OH^- \rightleftarrows Ar\bar{C}HCl + H_2O \qquad (69a)$$

$$Ar\bar{C}HCl + ArCH_2Cl \rightarrow Ar\dot{C}HCl + ArCH_2Cl^{\bullet -} \qquad (69b)$$
(V)

$$ArCH_2Cl^{\bullet -} + O_2 \rightarrow ArCH_2Cl + O_2^{\bullet -} \qquad (69c)$$

$$Ar\dot{C}HCl + O_2 \rightarrow ArCH(O_2\bullet)Cl \qquad (69d)$$

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*However, in one case, a carbanion (isolated as the sodium salt) has been shown to be rapidly converted to the hydroperoxide in good yield.

$$ArCH(O_2\cdot)Cl + Ar\bar{C}HCl \rightarrow ArCH(O_2^-)Cl + Ar\dot{C}HCl \quad (69e)$$

$$ArCH(OH^-)Cl + H_2O \rightarrow ArCH(O_2H) + OH^- \quad (69f)$$

$$ArCH(O_2H)Cl + Ar\bar{C}HCl \rightarrow ArCH(O^-)Cl + ArCH(OH)Cl \quad (69g)$$

$$ArCH(OH)Cl + OH^- \rightarrow ArCHO + Cl^- + H_2O \quad (69h)$$

$$ArCH(O^-)Cl \rightarrow ArCHO + Cl^- \quad (69i)$$

Oxygen could block stilbene formation (eq 66) by removing an electron from the radical anion (V) giving starting material (eq 69c). Therefore, the pathway giving stilbene would be replaced by the oxidation pathway, giving the stilbene oxides; this could explain the slower rate of reaction in the presence of oxygen.

An alternate to the initiation steps shown (eq 69b, c) might be:

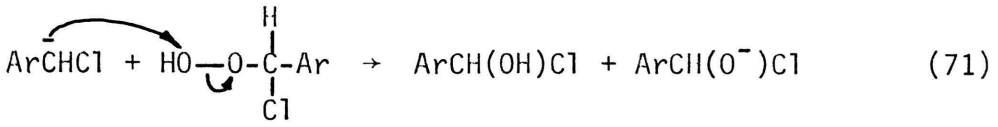
$$Ar\bar{C}HCl + O_2 \rightarrow Ar\dot{C}HCl + O_2^{\cdot -} \quad (69j)$$

This is just the sum of the reactions represented by eqs 69b and 69c. However, for the case of 2-nitropropane, the initiation seems to require both 2-nitropropane and 2-nitro-2-propyl anion; the anion alone is stable to oxygen.[29] It is noteworthy that solutions of 2-nitro-2-propyl anion and p-nitrobenzyl chloride are not stable to oxygen.[29] The 2-nitro-2-propyl anion is oxidized (eq 68), but the p-nitrobenzyl chloride is not consumed, indicating that p-nitrobenzyl chloride is acting to initiate the oxidation by accepting an electron from the anion (eq 70).[29]

$$Me_2\bar{C}NO_2 + ArCH_2Cl \rightarrow Me_2\dot{C}NO_2 + ArCH_2Cl^{\bullet -} \qquad (70)$$

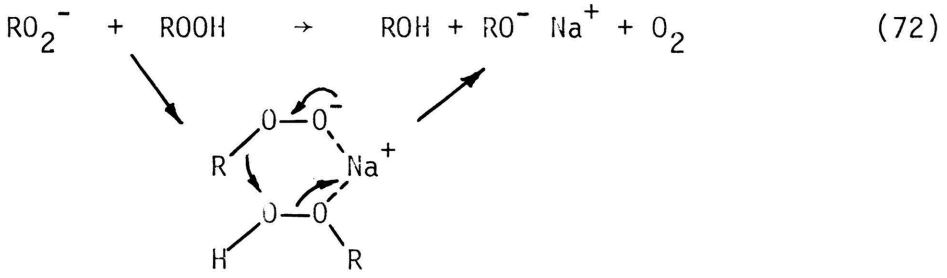
Therefore, p-nitrobenzyl chloride has been shown to be a good electron acceptor.

The disappearance of the hydroperoxide intermediate (eq 69g) can be explained by attack of the carbanion on the oxygen with the lower electron density.[52]



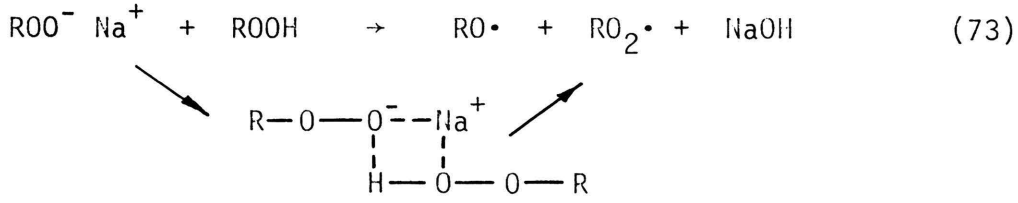
$$ArCHCl + HO{-}O{-}\underset{\displaystyle Cl}{\overset{\displaystyle H}{C}}{-}Ar \rightarrow ArCH(OH)Cl + ArCH(O^-)Cl \qquad (71)$$

The O—O linkage might be broken in other ways; either a homolytic or heterolytic cleavage is possible. The following homolytic mechanism[53] has been suggested.



$$RO_2^- + ROOH \rightarrow ROH + RO^- Na^+ + O_2 \qquad (72)$$

Heterolytic cleavage[53] from sodium salts of hydroperoxides is represented by eq 73.



$$ROO^- Na^+ + ROOH \rightarrow RO\bullet + RO_2\bullet + NaOH \qquad (73)$$

Such cleavage may be assisted by metal ions, at concentrations as low as 10^{-8} M;[54] low concentrations have been shown to be optimal for catalyzing autooxidations.[43] These trace metal ions are present in basic solutions as contaminants, although their influence is generally not recognized.[54]

In the complete absence of molecular oxygen, the fate of the radicals suggested in eq 69 would be different. p-Nitrobenzyl chloride radical anions (V) could decay to p-nitrobenzyl radicals (VI) and chloride ions; the radical (VI) would be free to couple with the carbanion of (I), as suggested in eq 66. The coupling of (VI) with α-chloro-p-nitrobenzyl radical (eq 62) is also a possibility.

The formation of the dinitrostilbene oxides (III) are less readily explainable. Although the formation of the dinitrostilbene (II) does not involve either a net oxidation or reduction, the formation of (III) is an oxidative process (eq 74). Only small amounts of reduced products (p-nitrotoluene) are detected (Table XIII).

$$2\ ArCH_2Cl + 4\ OH^- \rightarrow ArCH\overset{O}{\diagup\diagdown}CHAr + 3\ H_2O + 2\ Cl^- + 2e^- \quad (74)$$

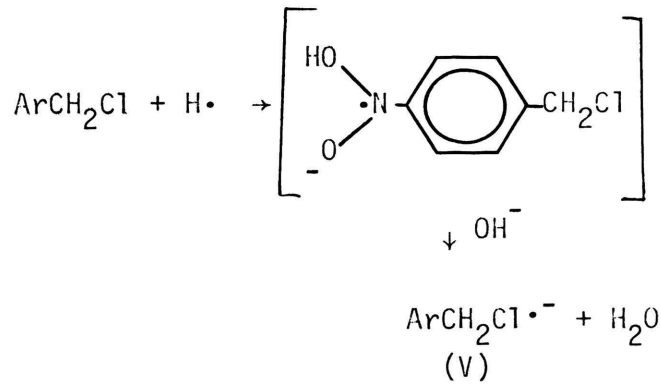
The actual mode of production of the stilbene oxides (III) is not clear; one possibility is the reaction of water with α-chloro-p-nitrobenzyl radical (eq 75), giving p-nitrobenzaldehyde.

$$Ar\dot{C}HCl + H_2O \rightarrow ArC(OH)HCl + H\cdot \quad (75a)$$

$$ArC(OH)HCl + OH^- \rightarrow ArCHO + Cl^- + H_2O \quad (75b)$$

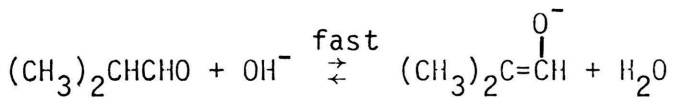
$$Ar\dot{C}HCl + H_2O \quad ArCH_2Cl + \cdot OH \quad (75c)$$

The hydrogen atom would presumably serve to generate additional p-nitrobenzyl chloride radical anions (V).

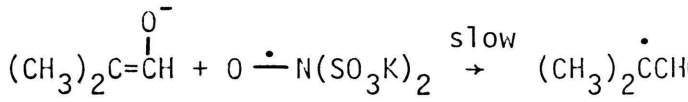


(76)

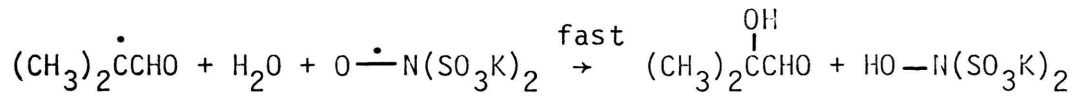
The reaction of a radical with water to abstract a hydroxyl radical may seem strange; however, if the radical did abstract a hydrogen atom, the result would be to regenerate p-nitrobenzyl chloride (eq 75c). An example of abstraction of a hydroxyl radical is the oxidation of isobutryaldehyde by Fremy's salt in basic solution.[55]



(77a)



(77b)



(77c)

Because the amount of the dinitrostilbene oxides formed in the absence of oxygen is similar to that of the dinitrostilbene, it seems more likely that the stilbene arises from the coupling (eq 78) of the p-nitrobenzyl radical (VI) with the carbanion of (I), as was suggested

in equation 66, rather than with an α-chloro-p-nitrobenzyl radical (eq 62).

$$\underset{(VI)}{ArCH_2\cdot} + Ar\bar{C}HCl \rightarrow ArCH_2CHClAr^{\cdot -} \qquad (78)$$

If the α-chloro-p-nitrobenzyl radical reacts with water in a solvent cage, giving p-nitrobenzaldehyde (eq 75), then very little of it could react with p-nitrobenzyl radical as suggested in eq 62. The same reasoning would apply to the formation of p,p'-dinitrotolane. It seems unlikely that a significant number of α-chloro-p-nitrobenzyl radicals could dimerize. A more likely reaction would be between the radical and the carbanion of (I).

$$Ar\dot{C}HCl + Ar\bar{C}HCl \rightarrow ArCHClCHClAr^{\cdot -} \qquad (79a)$$

$$ArCHClCHClAr^{\cdot -} + 2\ OH^- \rightarrow ArC{\equiv}CAr + 2\ Cl^- + 2\ H_2O + e^- \qquad (79b)$$

6. Effect of Added Dinitrobenzenes. The addition of m- and p-dinitrobenzene[28] to a basic solution of p-nitrobenzyl chloride brought about an intense red color which was destroyed upon acidification. With p-dinitrobenzene (p-DNB), a shoulder at 515 nm is observed in the visible spectrum immediately after mixing. The addition of either of the dinitrobenzenes caused a decrease in the amount of product which precipitated from the reaction mixture. For an equimolar mixture of p-nitrobenzyl chloride and m- and p-dinitrobenzene, the weight of precipitates were 64% and 46%, respectively of that observed in the absence of the dinitrobenzenes. The

precipitates also contained more unidentified material than that obtained from the reaction of p-nitrobenzyl chloride alone.

The relative rates of reaction, as monitored by chloride titration (Tables XIV-XVI) were in the order: no dinitrobenzene < p-dinitrobenzene < m-dinitrobenzene. The enhanced rate of reaction was surprising in view of the lesser amount of precipitate and the greater amount of unidentified material formed in the presence of the dinitrobenzenes. It was felt that if a radical ion mechanism was operating, such as suggested in eq 66, then the rate of reaction should be much slower, and little or no p,p'-dinitrostilbene would be formed.

The precipitate from the reaction of p-nitrobenzyl chloride and hydroxide ion with added p-dinitrobenzene (Table XVII) showed at least nine spots by tlc; cis- and trans-p,p'-dinitrostilbene oxides and p,p'-dinitrobibenzyl, as well as p,p'-dinitrostilbene were observed by both tlc and glc.

An additional major spot was observed in the precipitate with an R_f value characteristic for both p-dinitrobenzene and for p,p'-dinitrotolane, which unfortunately, have almost identical R_f values. However, the amount of p-dinitrobenzene found in the precipitate amounted to only 1% (recovered); almost all of the p-dinitrobenzene was in the extract of the filtrate. Therefore, some p,p'-dinitrotolane might also have been present.

Comparison of the products for this case with those for the reaction with no dinitrobenzene (Table XIII) shows that p-DNB reduced the amount of the stilbene by about 70%; the stilbene oxides were

Table XIV

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in 50% Aqueous Dioxane at 25°C, Run 52

0.01 M p-Nitrobenzyl Chloride

0.10 M NaOH

Time (sec)	1800	3600	5400	7200	9000
Reaction (%)	15.3	30.5	41.2	51.0	58.9
$k_2 \times 10^4$	9.24	10.28	10.05	10.21	10.20
(M^{-1} sec^{-1})			$\bar{k} = 10.00 \times 10^{-4}$		

Table XV

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion with Added p-Dinitrobenzene in 50% Aqueous Dioxane at 25°C, Run 53

0.01 M p-Nitrobenzyl Chloride

0.01 M p-Dinitrobenzene

0.10 M NaOH

Time (sec)	1800	3600	5400	7200	9000
Reaction (%)	21.0	40.6	53.0	62.6	70.8
$k_2 \times 10^4$	13.25	14.60	14.38	14.10	14.29
(M^{-1} sec^{-1})			$\bar{k} = 14.12 \times 10^{-4}$		

Table XVI

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion with Added m-Dinitrobenzene in 50% Aqueous Dioxane at 25°C, Run 54

0.01 M p-Nitrobenzyl Chloride

0.01 M m-Dinitrobenzene

0.10 M NaOH

Time (sec)	1800	3600	5400	7200	9000
Reaction (%)	30.2	50.6	64.8	73.7	82.5
$k_2 \times 10^4$	20.30	20.10	19.60	19.42	20.44
(M^{-1} sec^{-1})			$\bar{k} = 19.79 \times 10^{-4}$		

Table XVII

Reaction Products of p-Nitrobenzyl Chloride and Hydroxide Ion with Added p-Dinitrobenzene in 50% Aqueous Dioxane (Solutions Degassed by 3 Freeze-Thaw Cycles Before Mixing)

0.01 M p-Nitrobenzyl Chloride

0.01 M p-Dinitrobenzene

0.10 M NaOH

Compound	% Yield
cis-p,p'-dinitrostilbene	5.4
trans-p,p'-dinitrostilbene	10.4
cis- and trans-p,p'-dinitrostilbene oxides	22.0
p,p'-dinitrobibenzyl	10.5
p-nitrotoluene	7.7
p-nitrobenzyl alcohol	18.7
p-nitrobenzaldehyde	1.6
p-nitrobenzene (recovered)	62.0

decreased by about 50%. These decreases were accompanied by a six fold increase in p-nitrobenzyl alcohol. The greatest difference is in the amount of p-nitrotoluene (7.7%), and in the p,p'-dinitrobibenzyl (10.5%); the bibenzyl was not detected in the experiment with p-nitrobenzyl chloride alone (Table XIII). Both p-nitrotoluene and p,p'-dinitrobibenzyl could arise from reactions of p-nitrobenzyl radical (VI).[30]

$$\underset{\text{(VI)}}{ArCH_2\cdot} + SH \rightarrow ArCH_2 + S\cdot \qquad (80a)$$

$$2\ ArCH_2\cdot \rightarrow ArCH_2CH_2Ar \qquad (80b)$$

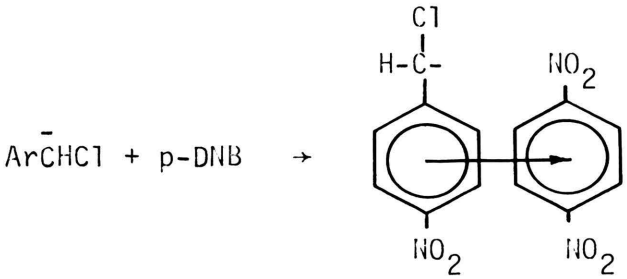
SH = solvent molecule

It is also possible that the p-nitrobenzyl radical could be a source of p-nitrobenzyl alcohol.

$$ArCH_2\cdot + H_2O\ (\text{or } \cdot OH) \rightarrow ArCH_2OH + H\cdot \qquad (81)$$

An obvious difference in the reaction products with p-DNB is the greater amount of reduced products (p-nitrotoluene and p,p'-dinitrobibenzyl); in this case, the amount of oxidation (production of the stilbene oxides) is approximately equal to that of reduction. With p-nitrobenzyl chloride alone (Table XIII), only traces of reduced products (p-nitrotoluene) were detected. p-Nitrobenzyl radical could only undergo reactions giving the reduction products (eq 80a and 80b) if the competing reaction with the carbanion (eq 78) was not

occurring. This would be possible if the concentration of the carbanion was low. The band at 515 nm in the visible spectrum[56]* of the reaction mixture may be due to a charge transfer complex between the carbanion of p-nitrobenzyl chloride and p-DNB; such a complex, if formed to any substantial degree, would lower the effective concentrations of both the carbanion and the dinitrobenzene.



(82)

A lower effective concentration of the dinitrobenzene would explain why it was not as effective as expected[28,31] in suppressing the formation of p,p'-dinitrostilbene.

7. Electron Spin Resonance. Electron spin resonance (ESR) has been widely used as a tool for the study of radical intermediates in the reactions of nitroaromatic compounds.[29,44] It was felt that it might be possible to detect radicals during the p-nitrobenzyl chloride--p,p'-dinitrostilbene transformation if the proper conditions were chosen. A high initial concentration of reactants, and a solvent system in which the products were fairly soluble should favor detection of such intermediates, if present.

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*Spectroscopic evidence for intermediate complexes of this type has been presented.

Initial studies with p-nitrobenzyl chloride were made in 50% aqueous dioxane; no ESR signal was detected. However, with added p-DNB, an ESR signal was readily detected (see Figure 2). This presumably was the signal of the p-dinitrobenzene radical anion ($p\text{-}DNB^{\bullet -}$).[29]

An ESR signal was obtained for p-nitrobenzyl chloride in ethanolic NaOH (Figure 3), and in 80% DMF--20% methanol with sodium methoxide as the base. In both cases, the signal presisted for a long period of time (the signal was undiminished even after the products had precipitated). Repeated scans, taken immediately after mixing, showed that the signal increased with time to a maximum. This is an indication that the signal is not of a reactive intermediate, but is probably a radical signal associated with the product, presumably the p,p'-dinitrostilbene radical anion.

The ESR signal from the reaction in ethanol (Figure 3), was poorly resolved due to dielectric loss.* The overmodulated signal (Figure 4), shows three peaks; this is an indication that the signal is of a species with an electron on a nitrogen atom. Nitrogen has a nuclear spin of I = 1; therefore, it gives three resonance lines.

$$N = 2\ I + 1 \qquad (83)$$

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*Solutions which are not ideal for ESR studies include aqueous solutions, solutions containing alcohols, and also basic solutions. Such samples must be run in very small sampling tubes, and at high power levels; poor signals result, due to poor tuning of the ESR cavity.

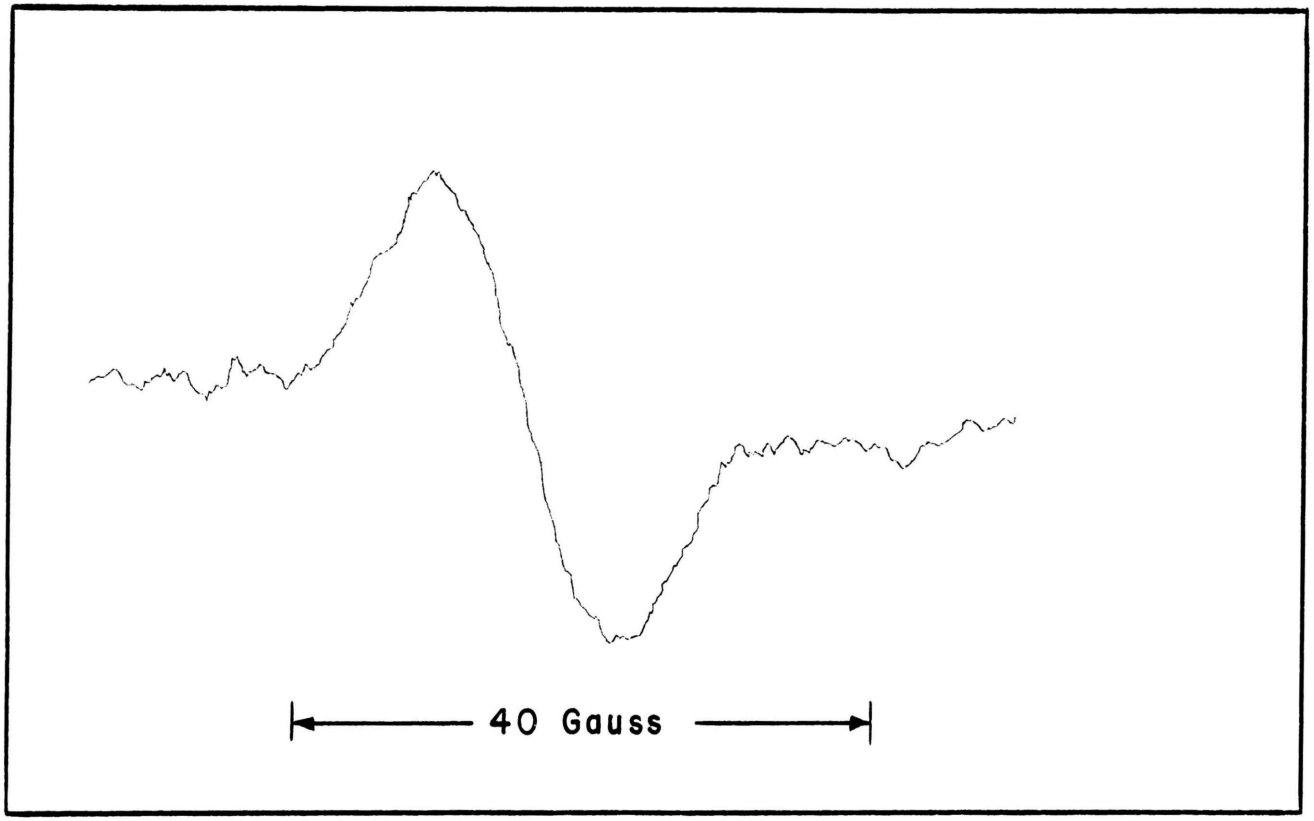


Figure 2. ESR signal obtained from the reaction of p-nitrobenzyl chloride and sodium hydroxide with added p-DNB in 50% aqueous dioxane

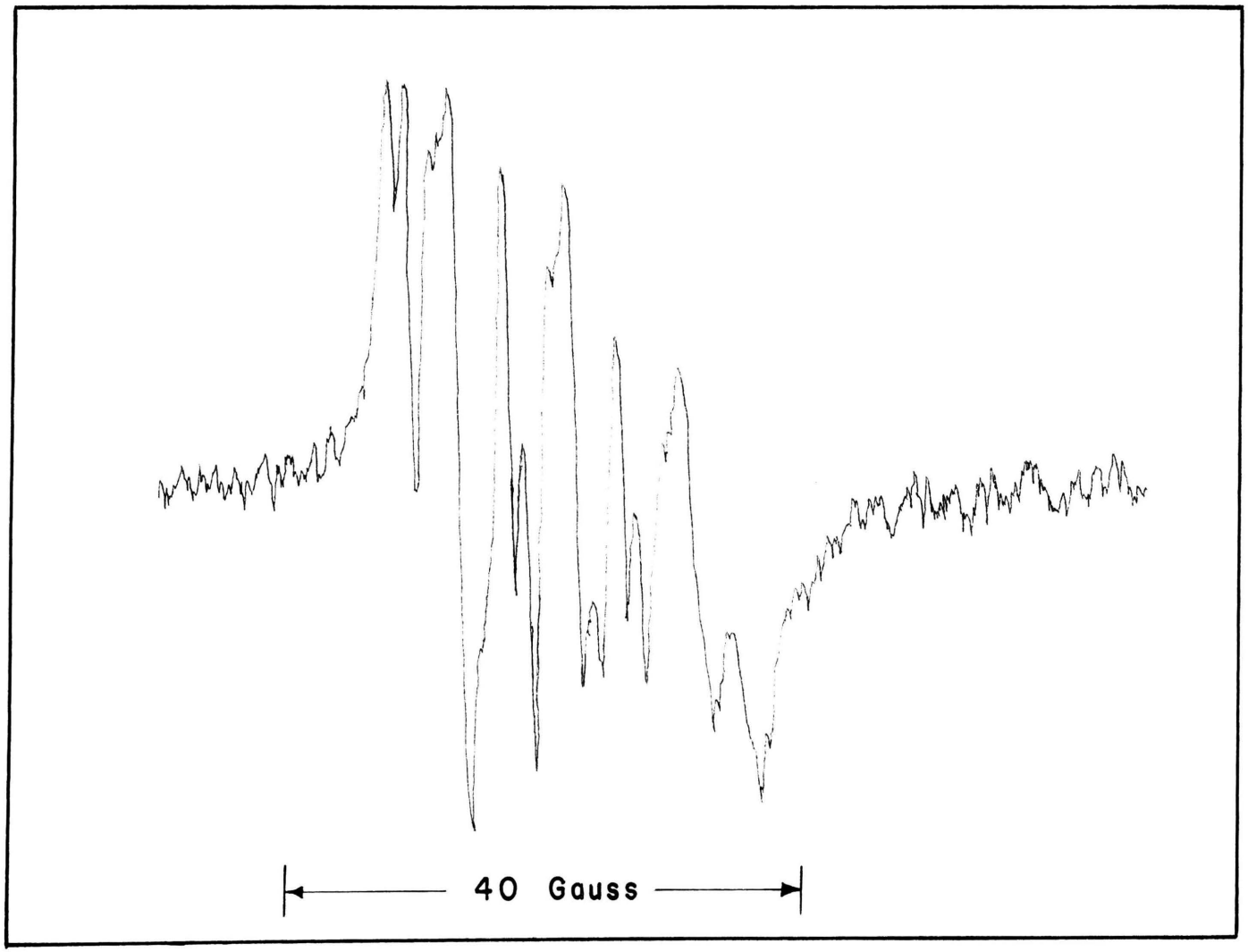


Figure 3. ESR signal obtained from reaction of p-nitrobenzyl chloride in ethanolic sodium hydroxide

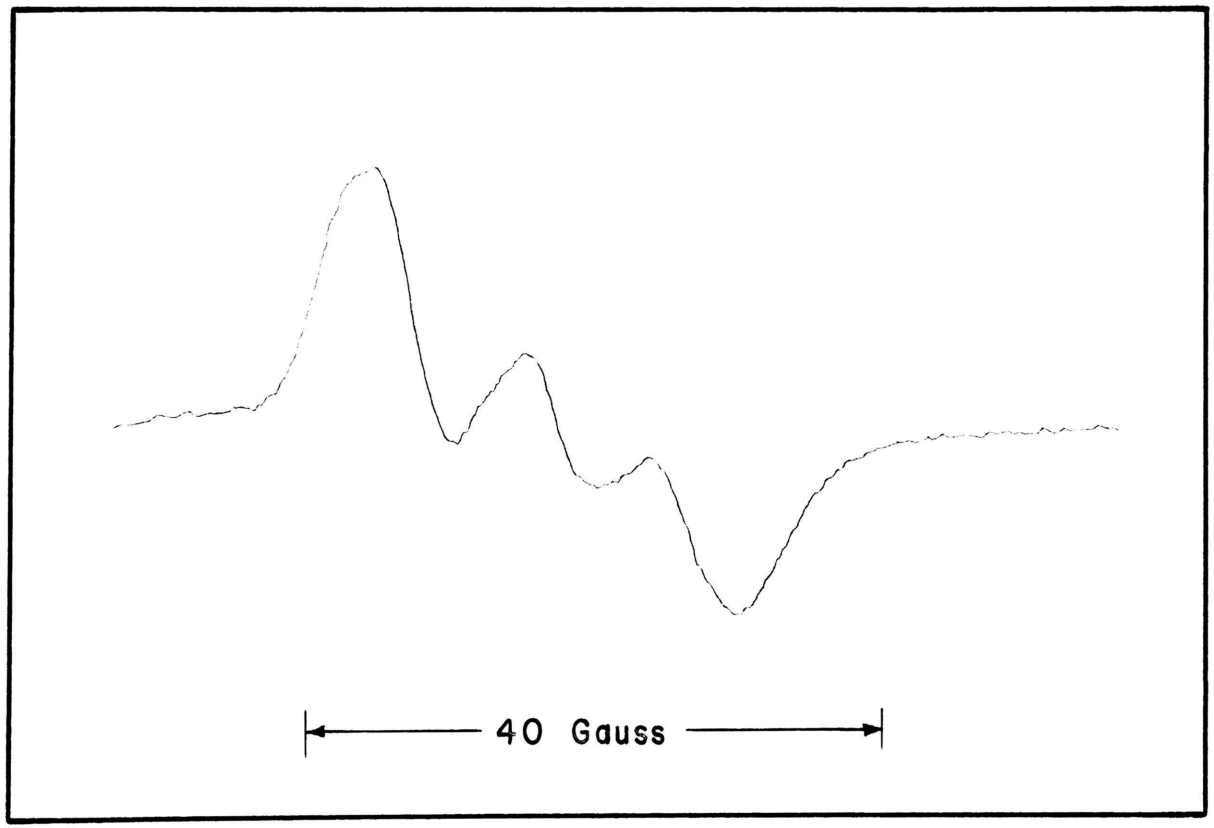


Figure 4. ESR signal (overmodulated) obtained from reaction of p-nitrobenzyl chloride in ethanolic sodium hydroxide

Although the observation of ESR signals does not constitute proof that the products are produced by radicals, it tends to support such a hypothesis, and it detracts from a totally ionic mechanism.

8. Effect of Added di-t-Butyl Nitroxide. Initial studies with a large amount of di-t-butyl nitroxide[36,37] added to the reaction of p-nitrobenzyl chloride and hydroxide ion indicate that the nitroxide is completely effective in preventing formation of p,p'-dinitrostilbene. However, smaller amounts seemed only to retard its formation. Therefore, a series of experiments using different amounts of the nitroxide were run (Table XVIII) to determine the amount necessary to inhibit completely the formation of the stilbene.

It is seen that approximately 40 mole% of the nitroxide is necessary to stop the formation of p,p'-dinitrostilbene. For the cases in which no stilbene was formed, di-t-butyl nitroxide are given in Tables XIX and XX for the reaction in the complete absence of oxygen. The first case (Table XIX) is for insufficient nitroxide; the second (Table XX) is for excess nitroxide.

The rate of the reaction of p-nitrobenzyl chloride with hydroxide ion is retarded strongly in the presence of added nitroxide (Figure 5); an induction period is observed during which no p,p'-dinitrostilbene is formed. The addition of small amounts of the nitroxide complicates the kinetics. The sigmoid shape of the curves (Figure 5), indicates a period of inhibition, which varies with the amount of nitroxide added. The addition of 5 mole% nitroxide caused the half-life of the reaction to be doubled; for 13 mole%, the half-life is 3.5 times as great as with no nitroxide. A peculiar feature is that

Table XVIII

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion with Different Concentrations of Di-t-butyl Nitroxide in 50% Aqueous Dioxane

0.01 M p-Nitrobenzyl Chloride

0.10 M NaOH

Reaction Time: 24 hr

Molarity of Nitroxide	Weight of Precipitate in Reaction Mixture	Yield of p-Nitrobenzyl Alcohol	Unreacted p-Nitrobenzyl Chloride
0.000	116.9 mg	3.6%	none
0.001	90.1 mg	11.6%	none
0.002	71.8 mg	18.2%	3.3%
0.003	57.4 mg	43.4%	5.6%
0.004	43.3 mg*	45.5%	7.2%
0.005	46.3 mg*	--	9.0%
0.010	40.0 mg*	49.9%	13.3%

*precipitate contained no p,p'-dinitrostilbene, but consisted entirely of cis- and trans-p,p'-dinitrostilbene oxides.

Table XIX

Reaction Products of p-Nitrobenzyl Chloride and Hydroxide Ion with Added Di-t-butyl Nitroxide in 50% Aqueous Dioxane (Solutions Degassed by 5 Freeze-Thaw Cycles before Mixing)

0.01 M p-Nitrobenzyl Chloride

0.0010 M Di-t-butyl Nitroxide

0.10 M NaOH

Reaction Time: 24 hr

Compound	% Yield
cis-p,p'-dinitrostilbene oxide	22.9
trans-p,p'-dinitrostilbene oxide	17.3
cis-p,p'-dinitrostilbene	19.1
trans-p,p'-dinitrostilbene	16.2
p-nitrobenzyl alcohol	11.9
p-nitrobenzaldehyde	1.4
p-nitrotoluene	trace
p-nitrobenzyl chloride (unreacted)	trace

Table XX

Reaction Products of p-Nitrobenzyl Chloride and Hydroxide Ion with Added Di-t-butyl Nitroxide in 50% Aqueous Dioxane (Solutions Degassed by 5 Freeze-Thaw Cycles before Mixing)

0.01 M p-Nitrobenzyl Chloride

0.0055 M Di-t-butyl Nitroxide

0.10 M NaOH

Reaction Time: 24 hr

Compound	% Yield
cis-p,p'-dinitrostilbene oxide	19.0
trans-p,p'-dinitrostilbene oxide	15.3
p-nitrobenzyl alcohol	49.0
p-nitrobenzaldehyde	5.9
p-nitrobenzyl chloride (unreacted)	9.3
p-nitrotoluene	trace

Table XXI

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion with Added Di-t-butyl Nitroxide in 50% Aqueous Dioxane at 25°C, Run 88

0.01 M p-Nitrobenzyl Chloride

0.0013 M Di-t-butyl Nitroxide

0.10 M NaOH

Time (sec)	1800	5400	5000	12600	16200	19800
Reaction (%)	2.9	8.2	14.1	20.3	26.2	34.6
Time (sec)	23400	27000	34200	39600	46800	
Reaction (%)	44.0	55.2	73.0	80.0	87.4	

Table XXII

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion with Added Di-t-butyl Nitroxide in 50% Aqueous Dioxane at 25°C, Run 89

0.01 M p-Nitrobenzyl Chloride

0.0005 M Di-t-butyl Nitroxide

0.10 M NaOH

Time (sec)	1800	5400	9000	12600	16200	19800
Reaction (%)	4.2	11.2	25.5	44.5	58.5	65.4
Time (sec)	23400	27000	34200	39600	46800	
Reaction (%)	72.0	78.0	86.4	92.6	92.6	

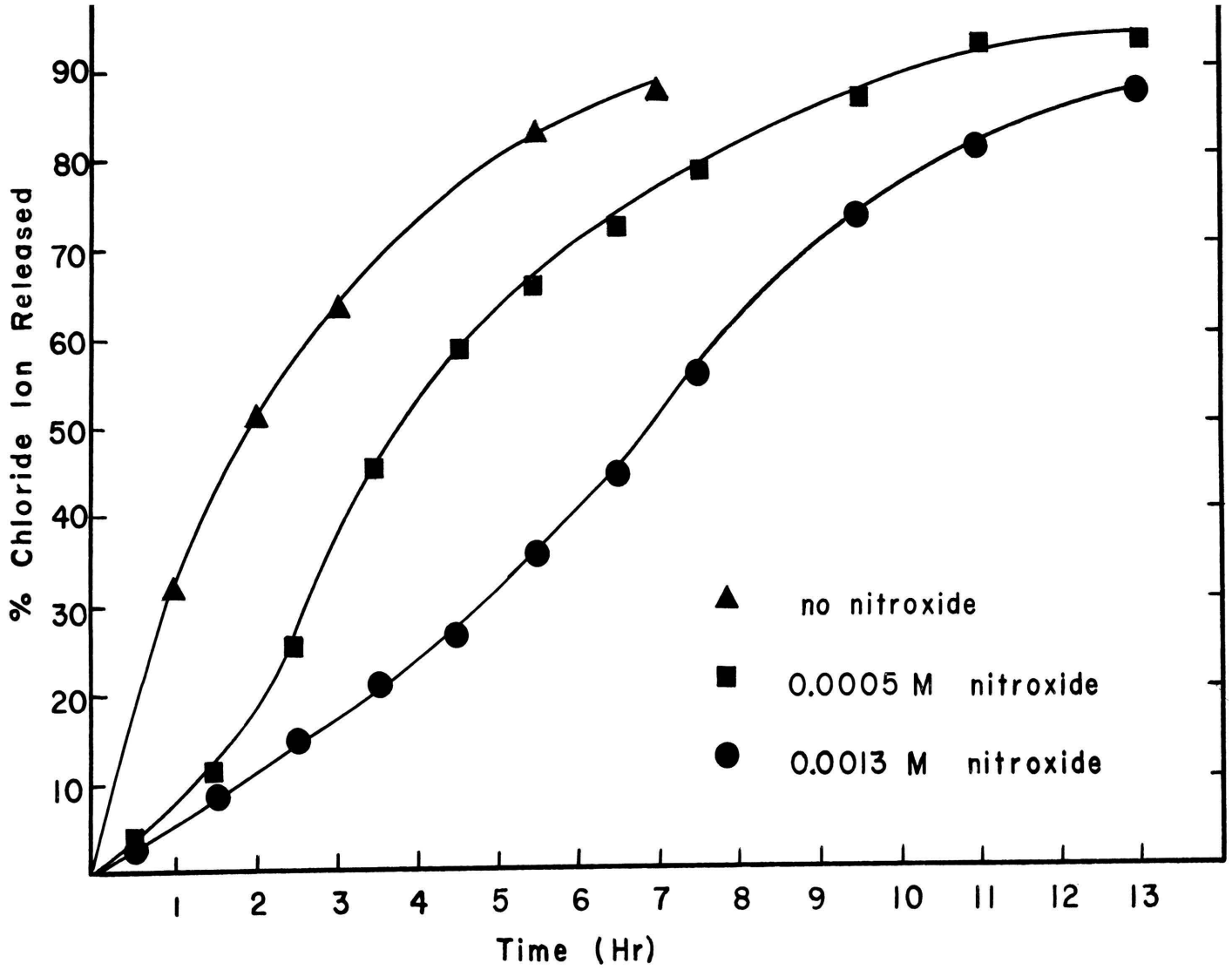


Figure 5. Plot of % chloride ion released vs time for reaction of 0.01 M p-nitrobenzyl chloride and 0.10 M NaOH in 50% aqueous dioxane at 25°C

the curves level off abruptly before reaching 100% reaction; this is reflected in the amount of unreacted p-nitrobenzyl chloride found after 24 hr in the reaction products.

The slower rate of reaction in the presence of di-t-butyl nitroxide indicates that it inhibits the formation of the stilbene, allowing other transformations which occur by slower pathways to predominate. Increasing the amount of nitroxide causes a decrease in p,p'-dinitrostilbene, and an increase in p-nitrobenzyl alcohol. The latter product may result from a nucleophilic displacement on p-nitrobenzyl chloride by hydroxide ion.

The formation of cis- and trans-p,p'-dinitrostilbene oxides in the presence of excess nitroxide probably occurs through p-nitrobenzaldehyde as an intermediate; the stilbene oxides are formed readily from the reaction of p-nitrobenzaldehyde and p-nitrobenzyl chloride and hydroxide ion in the presence of excess nitroxide. If the α-chloro-p-nitrobenzyl radical (eq 69b) is the intermediate through which p-nitrobenzaldehyde is formed, it should react primarily with water in the solvent cage (eq 75a, b) rather than with a nitroxyl radical. The hydrogen atom produced by this reaction would then be scavenged by the nitroxyl radical (eq 84).[55]

$$H\cdot + O\!-\!\dot{N}(Bu^t)_2 \rightarrow HON(Bu^t)_2 \qquad (84)$$

The scavenging of a hydrogen atom in this case would block the formation of another p-nitrobenzyl chloride radical anion (eq 76). The small decrease in the amount of the stilbene oxides produced (see Tables XIII, XIX, and XX) with increasing concentration of

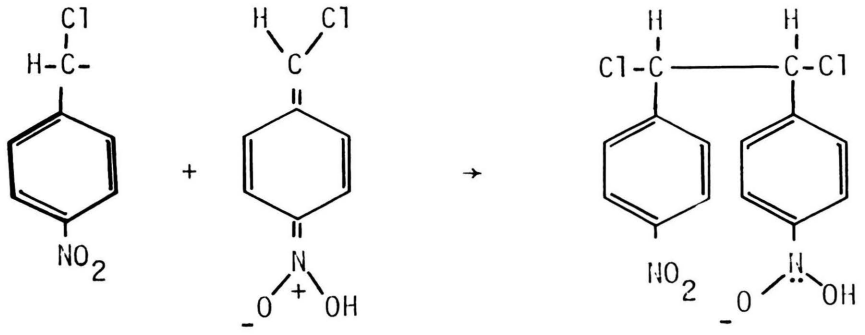
di-t-butyl nitroxide, may be the result of some of the α-chloro-p-nitrobenzyl radicals being scavenged (eq 85) by the nitroxide. Nitroxides couple with reactive radicals in the following manner.[57]

$$R\cdot + O\overset{\cdot}{-}N(Bu^t)_2 \rightarrow RON(Bu^t)_2 \qquad (85)$$

The absence of stilbene in the presence of excess nitroxide may be due to scavenging the p-nitrobenzyl radical (R = $ArCH_2\cdot$ in eq 85), or by an electron transfer reaction from p-nitrobenzyl chloride radical anion (eq 86).[55,58]

$$ArCH_2Cl^{\cdot -} + O\overset{\cdot}{-}N(Bu^t)_2 \rightarrow ArCH_2Cl + {}^{-}O-N(Bu^t)_2 \qquad (86)$$

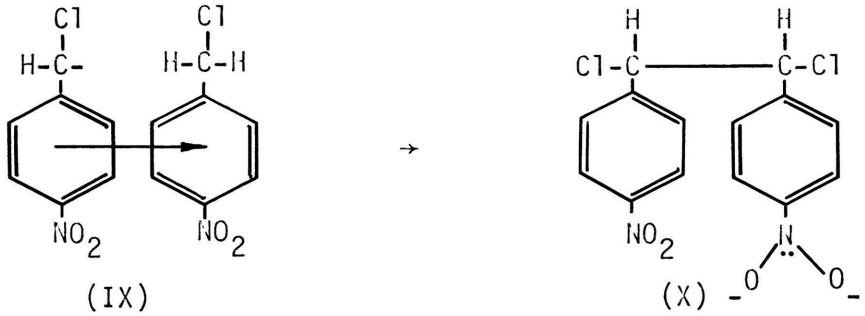
An alternate mechanism for the formation of p,p'-dinitrostilbene oxides could involve the formation of an adduct (VIII) of the carbanion of (I) with the aci-form of (I); similar adducts have been proposed as intermediates in the formation of p,p'-dinitrobibenzyl from p-nitrotoluene.[44]



(87)

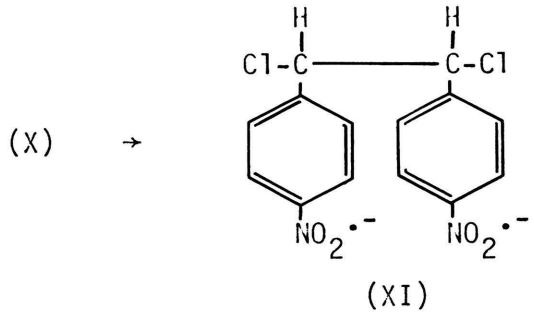
(VIII)

The adduct (VIII) or its conjugate base (X) may be formed through a preliminary charge-transfer complex (IX), followed by loss of a proton.[44,56]



(IX) (X) (88)

In basic solutions, the adduct (VIII) should be converted to (X); the latter intermediate might lose 2 chloride ions, giving the stilbene (II), or undergo intramolecular electron transfer to give the more stable intermediate (XI).



(X) (XI) (89)

An adduct similar to (X) (with $-\overset{+}{S}(Me)_2$ replacing Cl) has been considered by Russell and Danen as an intermediate in the formation of p,p'-dinitrostilbene from p-nitrobenzyldimethylsulfonium ion and hydroxide ion; however, the intermediate was discounted because oxygen blocked the formation of the stilbene.[29] In the case of the formation of p,p'-dinitrobibenzyl from p-nitrotoluene (eq 90), the reaction is an oxidation; oxygen increases the yield of the bibenzyl by accepting electrons, regenerating p-nitrotoluene (eq 91).[44]

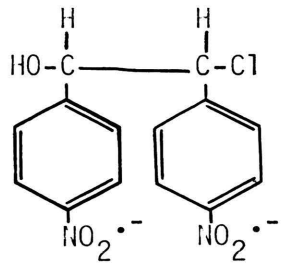
$$4\ ArCH_3 + 2\ B^- \rightarrow ArCH_2CH_2Ar + 2\ ArCH_3^{\bullet -} + 2\ BH \qquad (90)$$
(stable)

$$ArCH_3^{\bullet -} + O_2 \rightarrow ArCH_3 + O_2^{\bullet -} \qquad (91)$$

However, the formation of p,p'-dinitrostilbene from either p-nitrobenzyl chloride or p-nitrobenzyldimethylsulfonium ion is not an oxidative process. Therefore, oxygen should not increase the yield of the stilbene, but decrease it by converting intermediate (X) to (XI); which should be stable to expulsion of chloride ion (or dimethylsulfide).

The adduct (X) could be converted to the stilbene oxides by replacement of one chlorine by a hydroxyl group, followed by loss of two electrons, and then closure of the chlorohydrin intermediate to give the epoxide.

$$(XI) + OH^- \rightarrow$$



(XII) (92)

$$\downarrow\ 2\ A \quad (A = \text{electron acceptor})$$

$$ArCH\underset{\diagdown}{\overset{\diagup}{O}}CHAr \xleftarrow{OH^-} [ArCH(OH)CHClAr] + 2\ A^{\bullet -}$$

In the absence of oxygen as an electron acceptor, p-nitrobenzyl chloride might pick up an electron, giving the radical anion (V); (I) is known to be a good electron acceptor.[29]

$$(XII) + 2\ \underset{(I)}{ArCH_2Cl} \rightarrow ArCH(OH)CHClAr + 2\ \underset{(V)}{ArCH_2Cl^{\bullet -}} \qquad (93)$$

Thus, the production of the dinitrostilbene oxides could serve as a source of electrons, acting as the driving force for a radical anion mechanism in the production of (II).

$$\underset{(V)}{ArCH_2Cl^{\bullet -}} \rightarrow \underset{(VI)}{ArCH_2\bullet} + Cl^- \qquad (94a)$$

$$ArCH_2\bullet + Ar\bar{C}HCl \rightarrow ArCH_2CHClAr^{\bullet -} \qquad (94b)$$

$$ArCH_2CHClAr^{\bullet -} + OH^- \rightarrow ArCH{=}CHAr^{\bullet -} + Cl^- + H_2O \qquad (94c)$$

$$ArCH{=}CHAr^{\bullet -} + ArCH_2Cl \rightarrow \underset{(II)}{ArCH{=}CHAr} + ArCH_2Cl^{\bullet -} \qquad (94d)$$

According to eq 93, the formation of the stilbene oxides is accompanied by electron transfer to (I); a long kinetic chain length is therefore not necessary for the efficient production of (II); the chain propagation step (eq 94d) may be inefficient, or may not occur at all.

9. Mechanistic Conclusions. It is obvious from the preceding work that the base-induced reactions of p-nitrobenzyl chloride are complex. It does not seem likely that the production of (II) occurs solely by the previously proposed carbene pathway;[9] the possibility of more than one mode of production should be considered. Three types of mechanisms are to be considered: a strictly ionic mechanism, such as represented in equation 6, or one involving an

intermediate such as (IX), the carbene mechanism (eq 8), and those mechanisms involving radicals.

The strictly ionic mechanism (eq 6) would seem to be reasonable; however, if an alkylation-dehydrohalogenation mechanism is important for the production of (II) from (I), then it should also be an important process with p-nitrobenzyl bromide and p-nitrobenzyl iodide. Although the carbanions from p-nitrobenzyl bromide and p-nitrobenzyl iodide are formed more rapidly than the carbanion from p-nitrobenzyl chloride, it is reported that p,p'-dinitrostilbene is not formed from these halides.[17] The rate increase with light might be considered indicative of a radical process; however light catalysis of strictly ionic processes is not unusual for nitro-aromatic compounds.[59,60] Although oxygen would interfer in an alkylation-dehydrohalogenation mechanism by intercepting the carbanion, such a scheme is inconsistent with the complete absence of (II) in a reaction that is slowed by oxygen. The retardation of the rate and the change of products caused by the addition of di-t-butyl nitroxide might be explained by a side reaction of the carbanion with the nitroxide. If an appreciable amount of the carbanion was tied up or consumed in such a reaction, the pathway giving the stilbene (eq 6b) would be blocked. However, the magnitude of the rate retardation seems much too great for such an argument.

The carbene mechanism is attractive because of kinetic considerations, including the observed kinetic isotope effects. Oxygen could serve to block the formation of (II) by reacting with either the carbanion or the proposed p-nitrophenyl carbene. In a

like manner di-t-butyl nitroxide might interfere with the stilbene formation by reacting with the carbene, which presumably would be in a triplet state.[11] However, as in the case of the alkylation-dehydrohalogenation mechanism, the reaction with added nitroxide seems much too slow if this is the only pathway for stilbene formation. The main theoretical objection for the proposed carbene intermediate is the small amount of p-nitrobenzyl alcohol formed. Because the carbene is an electrophilic species,[61] the question remains why the carbene would attack the carbanion of (I) in preference to hydroxide ion, which is present at a much higher concentration.

Mechanisms involving radicals seem consistent with most of the experimental facts. The products, in the presence, and in the absence, of oxygen are explainable in terms of the radicals proposed. The most probable mode of initiation of a radical pathway, giving the proposed radicals, would involve a one electron transfer from the carbanion to a neutral molecule of p-nitrobenzyl chloride, as suggested in equation 69b.

$$ArCH_2Cl + OH^- \rightleftarrows Ar\bar{C}HCl + H_2O \qquad (69a)$$

$$Ar\bar{C}HCl + ArCH_2Cl \rightarrow Ar\dot{C}HCl + \underset{(V)}{ArCH_2Cl^{\bullet -}} \qquad (69b)$$

The fate of (V) would be loss of a chloride ion, giving p-nitrobenzyl radical (VI), which could couple with the carbanion, as suggested in equation 94b.

$$\underset{(V)}{ArCH_2Cl^{\bullet -}} \rightarrow ArCH_2\bullet + Cl^- \qquad (94a)$$

$$\underset{(VI)}{ArCH_2\bullet} + Ar\bar{C}HCl \rightarrow ArCH_2CHClAr^{\bullet -} \qquad (94b)$$

$$ArCH_2CHClAr^{\bullet -} + OH^- \rightarrow ArCH{=}CHAr^{\bullet -} + H_2O + Cl^- \qquad (94c)$$

$$ArCH{=}CHAr^{\bullet -} + ArCH_2Cl \rightarrow ArCH{=}CHAr + ArCH_2Cl^{\bullet -} \qquad (94d)$$

The α-chloro-p-nitrobenzyl radical could react with water in the solvent cage giving p-nitrobenzaldehyde (eq 75); the latter compound would be rapidly converted to the observed p,p'-dinitro-stilbene oxides (eq 5).

$$Ar\dot{C}HCl + H_2O \rightarrow ArCH(OH)Cl + H\bullet \qquad (75a)$$

$$ArCH(OH)Cl + OH^- \rightarrow ArCHO + H_2O + Cl^- \qquad (75b)$$

$$Ar\bar{C}HCl + ArCHO \rightarrow ArCH\overset{O}{\diagup\diagdown}CHAr + Cl^- \qquad (5)$$

The increase of the rate with illumination could be caused by an increase in the concentration of the radical anion (V).[29] However, the effect of light is not a large one, and the reaction precedes in total darkness; therefore, this information is inconclusive. Oxygen and di-t-butyl nitroxide would effectively block the production of the stilbene; both the carbanion and the radical (VI) are necessary in the pathway represented in equation 94b. An effective radical scavenger should block this pathway by coupling with the radical (VI).

The deuterium isotope effect observed could be explained if the coupling of the radical (VI) and the carbanion (eq 94b) were rate-determining. The chlorine kinetic isotope effect would presumably arise from loss of chloride ion from the radical anion (V), as suggested in equation 94a. The loss of the second chloride ion (eq 94c) should be a rapid, indiscriminate process, and cause a dilution of the isotope effect which occurs from the earlier step (eq 94a); this will dilute the chlorine kinetic isotope effect. The pathway, giving the dinitrostilbene oxides would also make a large contribution to the observed kinetic isotope effects. Because this pathway (eq 75) is dependent on the α-chloro-p-nitrobenzyl radical, a species that arises from a reaction of the carbanion (eq 69b), it should give a significant deuterium kinetic isotope effect. However, the loss of chloride ion in these steps (eq 75b, 5) should occur rapidly in comparison to the step for formation of the α-chloro-p-nitrobenzyl radical (eq 69b); therefore, these steps should also give a dilution of the chlorine kinetic isotope effect. Therefore, the only step that should give a significant chlorine kinetic isotope effect should be the one in which a chloride ion is lost from the radical anion (V); the other steps would only decrease the isotope effect observed. The main objection to the radical pathway is the intermediacy of the radical anion (V) in the presence of added dinitrobenzenes. In view of other experiments,[28,31] it would seem that the addition of p-DNB would completely inhibit the formation of the p,p'-dinitrostilbene if it is produced solely <u>via</u> a mechanism requiring the radical anion (V).

Because no one mechanism completely explains the total behavior of the system, it may be that (II) is formed by more than one pathway. Other experiments, such as spin trapping,[62] might give additional useful information, that would further clarify the mode of production of p,p'-dinitrostilbene.

B. Studies on p-Nitrobenzyldimethylsulfonium Salts

1. Reactions of p-Nitrobenzyldimethylsulfonium Tosylate with Hydroxide Ion. The behavior of various substituted benzyldimethylsulfonium salts with hydroxide ion,[21] is similar to that of substituted benzyl chlorides in basic media,[2a] in that the corresponding alcohols are formed in both reactions. A parallelism also exists for the reaction of p-nitrobenzyldimethylsulfonium tosylate with hydroxide ion and the reaction of p-nitrobenzyl chloride in basic media;[4,9,14] p,p'-dinitrostilbene is formed in both cases. Because of this similarity, the effect of oxygen and of added di-t-butyl nitroxide on the products of the reaction of the sulfonium salts were studied. The reaction of the sulfonium tosylate and hydroxide ion, without additives, was also studied for comparison purposes. The weight of the precipitate formed from the reaction of p-nitrobenzyldimethylsulfonium tosylate and hydroxide ion (0.1369 g) would account for the "quantitative yield" of p,p'-dinitrostilbene reported previously.[12,22] However, both tlc and the visible and ultraviolet spectra (DMF) indicate that the precipitate consisted of two different compounds: p,p'-dinitrostilbene and p,p'-dinitrostilbene oxide. The two bands at 368 nm and 290 nm correspond to a mixture of trans-p,p'-dinitrostilbene and trans-p,p'-dinitrostilbene oxide, and not to a mixture of cis- and trans-p,p'-dinitrostilbene. Pure trans-p,p'-dinitrostilbene in DMF has λ_{max} = 368 nm, and pure cis-p,p'-dinitrostilbene in DMF has λ_{max} = 320 nm.[63] Mixtures of the two isomers in DMF give one band, with the maxima between the two extreme

Table XXIII

Analysis of the Precipitates Obtained from the Reaction of p-Nitrobenzyldimethylsulfonium Tosylate and Hydroxide Ion at 60°

0.01 M p-Nitrobenzyldimethylsulfonium Tosylate

0.10 M NaOH

Weight of Precipitate Formed	Yield of p,p'-Dinitrostilbene Formed[c]	Yield of p,p'-Dinitrostilbene Oxide Formed[c]
0.1369 g	31.4	52.0
0.0826 g[a]	3.4	54.3
0.1328 g[b]	13.3	79.5

[a] run with an oxygen atmosphere; p-nitrobenzaldehyde (3.4% yield), and p-nitrobenzyl alcohol (11.0% yield) were also recovered from the filtrate.

[b] 0.0846 g of di-t-butyl nitroxide added (0.006 M)

values; the position of the maxima are approximately proportional to the relative amounts of the two isomers.

The "quantitative yield" of p,p'-dinitrostilbene reported[12,22] and the results that we have obtained are difficult to reconcile, as the experimental conditions that we employed were identical to those reported.[12] The great range (over 100 degrees) of the melting point of the product has been explained as being the result of a mixture of the two isomers of the stilbene.[12] The mixture was reportedly isomerized to the trans isomer by treating the precipitate with a catalytic amount of iodine in refluxing nitrobenzene.[12,22]

It seems possible that the nitrobenzene--iodine treatment was only a simple recrystallization; nitrobenzene is a good solvent for the recrystallization of p,p'-dinitrostilbene.[4] The trans isomer of p,p'-dinitrostilbene is very insoluble in most solvents, and would likely precipitate first from a mixture of solutes.

It is notable that p-nitrobenzyl alcohol and p,p'-dinitrostilbene oxide were isolated by column chromatography from the reaction of other p-nitrobenzylsulfonium salts and hydroxide ion.[13] Column chromatography was not employed in the case of p-nitrobenzyldimethylsulfonium tosylate.[12,22]

Both oxygen and di-t-butyl nitroxide showed significant effects on the amount of the stilbene produced, although not as drastic effects as in the case of p-nitrobenzyl chloride (Cf Tables XXI and XXII). The reaction of the sulfonium salt and hydroxide ion with added di-t-butyl nitroxide was visibly different from the reaction in the absence of that additive. In the latter case, the reaction was very

rapid, giving a precipitate shortly after the mixing of reactants. However, with the added nitroxide, the precipitate formed very slowly. The red color that formed upon mixing p-nitrobenzyldimethylsulfonium tosylate and hydroxide ion has been attributed to the ylide;[12] it faded quickly with the formation of the precipitate.

$$ArCH_2\overset{+}{S}(Me)_2 + OH^- \rightleftarrows \underset{\text{(red)}}{ArC\overset{-}{H}\overset{+}{S}(Me)_2} + H_2O \qquad (95)$$

For the reaction with added nitroxide, the red color faded very slowly, indicating that the concentration of the ylide remained relatively unchanged for a long period of time. This seems to indicate that the nitroxide strongly retards the rate of the reaction.

2. Reactions of p-Nitrobenzyldimethylsulfonium Bromide and Hydroxide Ion. The reactions of p-nitrobenzyldimethylsulfonium bromide were investigated, using the same procedures as those employed for the tosylate. The amount of di-t-butyl nitroxide was increased, to see if a greater amount would block completely the production of p,p'-dinitrostilbene. The use of excess di-t-butyl nitroxide was effective in blocking stilbene formation completely; the main by-product (found in the extract) was p-nitrobenzyl alcohol.

One pronounced difference between the products obtained from the reaction of the sulfonium salts and those from p-nitrobenzyl chloride is that the former give almost exclusively the trans isomers of both p,p'-dinitrostilbene and p,p'-dinitrostilbene oxide. It is possible that the difference observed in the case of the stilbene is due to the solvent. In water, the products precipitate very rapidly; in

Table XXIV

Analysis of the Precipitates Obtained from the Reactions of p-Nitrobenzyldimethylsulfonium Bromide and Hydroxide Ion at 60°

0.10 M NaOH

Concentration of Sulfonium Salt	Weight of Precipitate Formed	Yield of p,p'-Dinitrostilbene Formed[c]	Yield of p,p'-Dinitrostilbene Oxide Formed[c]
0.01 M	0.1246 g	36.9	42.8
0.10 M	1.3175 g	33.4	35.5
0.01 M[a]	0.0924 g	3.8	59.0
0.01 M[b]	0.0664 g	0.0	46.2

[a] run with an oxygen atmosphere

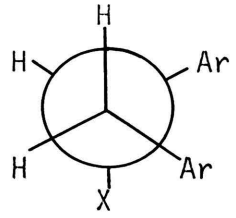
[b] 0.1050 g of di-t-butyl nitroxide added (0.010 M)

[c] predominantly the trans isomer

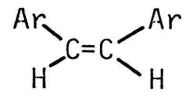
aqueous dioxane, they are held in solution for a much longer time. Solutions of both cis- and trans-p,p'-dinitrostilbene in DMF, have been observed to undergo isomerization, giving an equilibrium mixture of the two isomers. This has also been noticed for acetone solutions used for tlc.

If p,p'-dinitrostilbene is formed by an elimination from a bibenzyl intermediate, the less hindered isomer should be formed preferentially. A trans- elimination from the less hindered transition state would give the trans isomer.

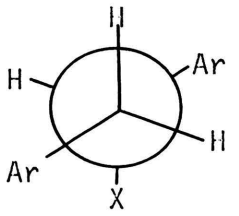
$X = \overset{+}{S}(Me)_2$ or Cl



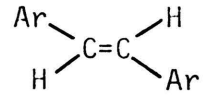
(more hindered)



(96a)



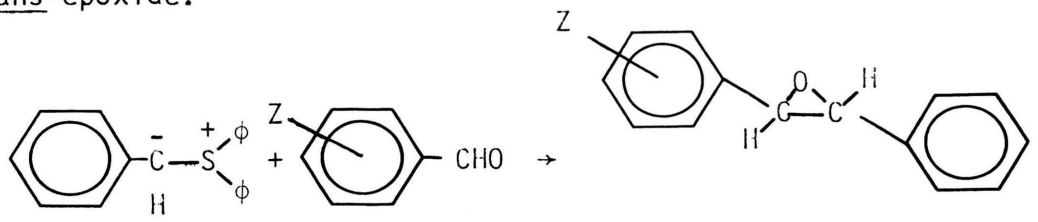
(less hindered)



(96b)

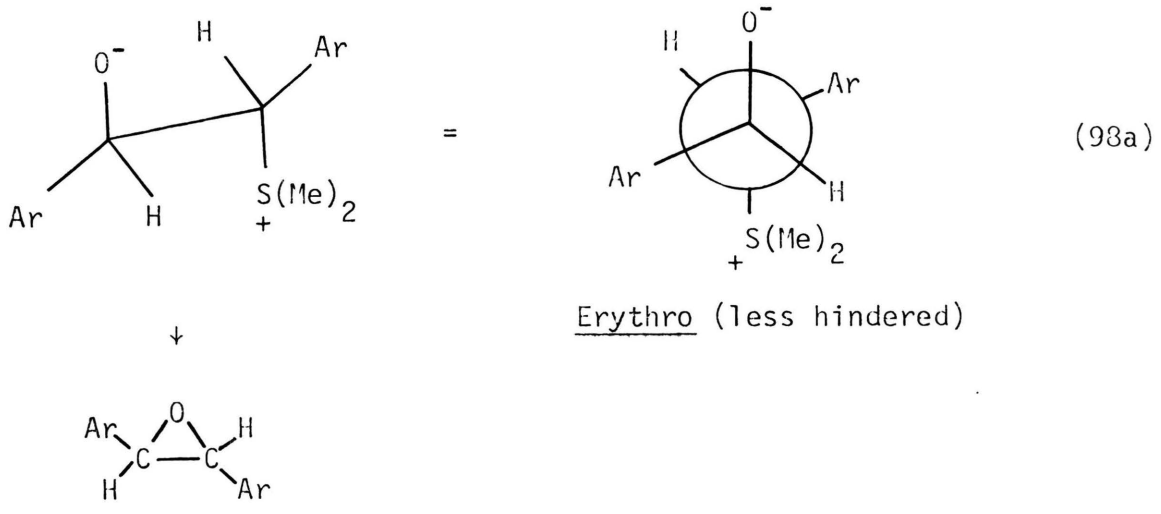
For a bulky group ($X = \overset{+}{S}(Me)_2$) one might expect the less hindered transition state (eq 96b) to predominate. However, for a group with a lesser steric requirement (X = Cl), the intervention of the more crowded transition state (eq 96a) leading to the cis-p,p'-dinitrostilbene is not excluded. The case of p,p'-dinitrostilbene oxide is

different; no cis-trans isomerization was observed. The detection of almost exclusive formation of the trans-p,p'-dinitrostilbene oxide is consistent with the results of condensing diphenylsulfonium benzylide with substituted benzaldehydes to give exclusively the trans-epoxide.[64]

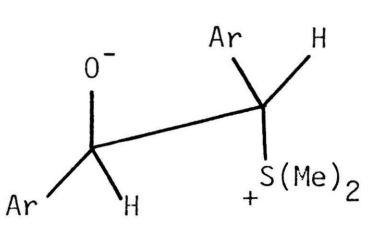


(97)

If p-nitrobenzaldehyde is an intermediate in the formation of trans-p,p'-dinitrostilbene oxide, a trans-elimination from the erythro intermediate adduct would give trans-p,p'-dinitrostilbene oxide (eq 98a), while the more hindered threo intermediate adduct would give the cis-epoxide (eq 98b).[64]



(98a)



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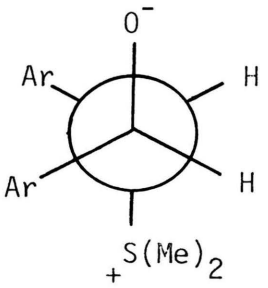
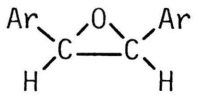


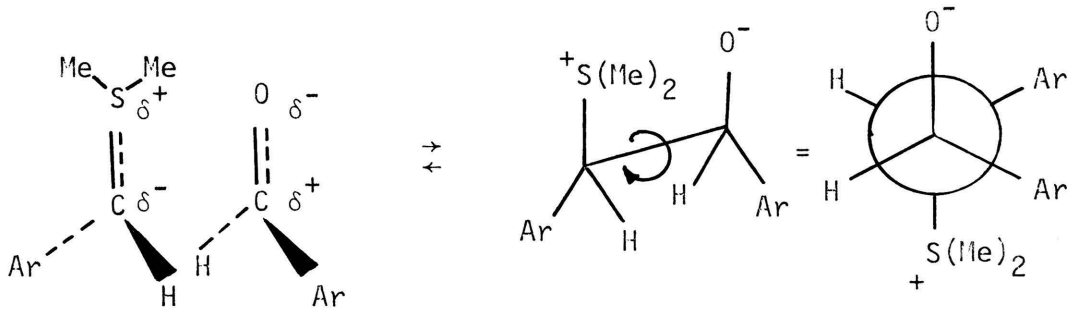
(98b)

Threo (more hindered)



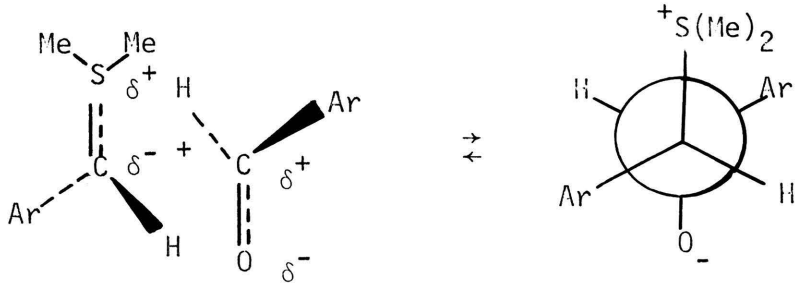
If attack of the ylide on the carbonyl carbon is reversible, then one would expect the trans isomer to be formed almost exclusively, because of the greater ease of elimination from the erythro adduct (eq 98a). However, if the addition step is not reversible, then the predominance of the trans isomer must be explained in terms of the steric factors that control the addition of the ylide to the carbonyl compound.

Two types of transition states are possible: an eclipsed conformation, and a staggered conformation. The eclipsed conformation could favor the approach with maximum electrostatic attraction between the charged groups, and minimum nonbonded interaction (eq 99); this would give the threo adduct, and ultimately the cis-p,p'-dinitrostilbene oxide.



(Type I) Threo (99)

The staggered conformation would be more probable in a polar solvent, e. g. water, where solvation would decrease the positive charge on sulfur.[65*] This would be accomplished through a less hindered approach.

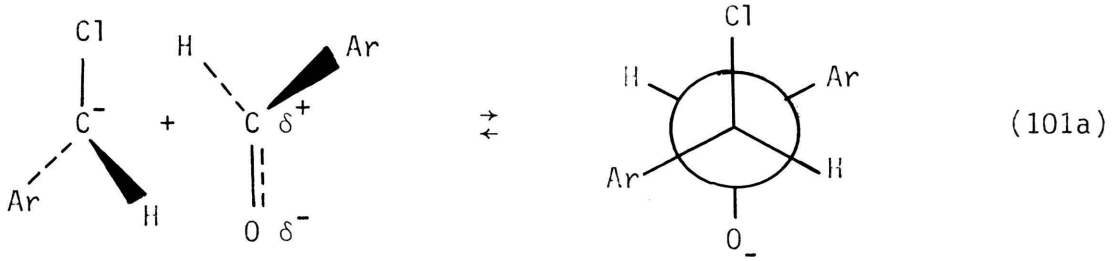


(Type II) Erythro (100)

In water, the staggered transition state (Type II) would be favored, because the electrostatic attraction between the positive sulfur and

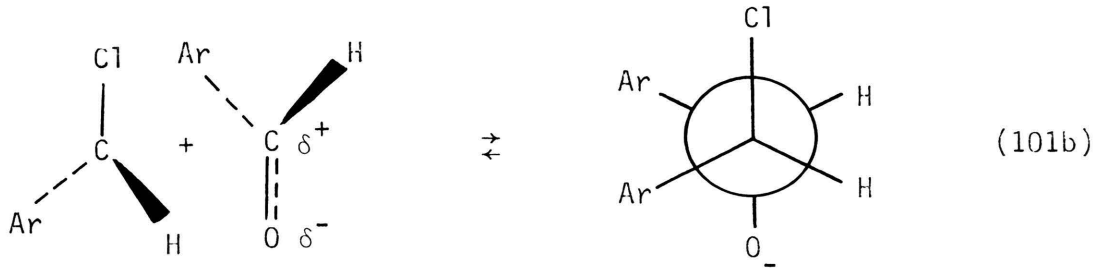
*A similar case is the addition of ylides to carbonyl compounds in the Wittig reaction. In non-polar solvents, a transition state like type 1 is postulated, while in polar solvents, or with added nucleophiles, a transition state of type II is considered more likely. This is reflected in a change of the products from the trans olefin to predominantly the cis olefin as the solvent becomes more polar.

the oxygen of the carbonyl group would be minimized. Thus, the predominance of the trans-p,p'-dinitrostilbene oxide in the case of the sulfonium salts is rationalized. For the case of p-nitrobenzyl chloride, the smaller size of the chlorine would lead to a less stereoselective adduct formation. A second difference is that the sulfur of the ylide would tend to accommodate the negative charge on the benzylic carbon; for the carbanion of p-nitrobenzyl chloride, the negative charge would be less delocalized.



(101a)

Erythro



(101b)

Threo

C. Studies on p-Nitrobenzyl Tosylate, Bromide, and Iodide

1. p-Nitrobenzyl Tosylate. The reaction of this compound with hydroxide ion in 50% aqueous dioxane led to a variety of products which are shown collectively in Table XXV.

The alcohol, which is the major product (~52%) is most probably produced by an S_N2 process. The stilbene oxides might arise from a condensation of the carbanion with p-nitrobenzaldehyde, which could be formed from the elimination of the anion of p-toluenesulfinic acid from the carbanion of the tosylate.[67*] However, no p-toluene-

(102)

sulfinic acid was detected in the reaction mixture. This may be because the acid does not survive under the reaction conditions. Presumably, it might be oxidized to p-toluenesulfonic acid, which was shown to be present.

The observed p,p'-dinitrostilbene (~3.5%) may be explained by any of the mechanisms already discussed.

2. p-Nitrobenzyl Bromide and p-Nitrobenzyl Iodide. A previous study of the reactions of both p-nitrobenzyl bromide and p-nitrobenzyl iodide with hydroxide ion in aqueous dioxane reported a quantitative yield on p,p'-dinitrobibenzyl ether; the reactions are reportedly unaffected by air.[17] In view of the effect of oxygen on the reactions

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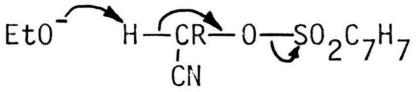
*Such an elimination has been observed for one substituted benzyl tosylate:



(where R = $O\text{-}NO_2C_6H_4$) .

Table XXV

Products from the Reaction of p-Nitrobenzyl Tosylate and Hydroxide Ion in 50% Aqueous Dioxane

0.01 M p-Nitrobenzyl Tosylate

0.10 M NaOH

Compound	% Yield
cis- and trans-p,p'-dinitrostilbene oxides[a,b]	~20.0
p,p'-dinitrostilbene[b]	~3.5
p-nitrobenzyl alcohol	52.3
p-nitrobenzaldehyde	2.0
p-nitrotoluene	0.2

[a] approximately equal amounts of each isomer

[b] estimated by tlc

of p-nitrobenzyl chloride (Table X) and p-nitrobenzyldimethylsulfonium salts (Tables XXIII and XXIV), a re-examination of the reactions of these halides was undertaken; the results are given collectively in Table XXVI. The precipitate formed (presumably the bibenzyl ether) was much less than that corresponding to a "quantitative yield". p-Nitrobenzyl alcohol was the major product, and was recovered by extraction of the filtrates.

The precipitates were shown to contain more than one component by tlc analysis; therefore, the figures in Table XXVI represent the maximum amount of p,p'-dinitrobibenzyl ether (if any) that may have been formed. p,p'-Dinitrostilbene was shown to be present in small amounts for the reaction of both p-nitrobenzyl bromide and p-nitrobenzyl iodide, but not for p-nitrobenzyl bromide with an oxygen atmosphere.

The complete analyses for the reactions of p-nitrobenzyl bromide with hydroxide ion, with and without an oxygen atmosphere, are given in Tables XXVII and XXVIII. The reaction products from p-nitrobenzyl iodide are very similar to those from p-nitrobenzyl bromide; these products were not analyzed further. One notices that the p-nitrobenzyl bromide--hydroxide ion reaction is not very sensitive to oxygen; by contrast, in the p-nitrobenzyl chloride system under identical conditions, the yield of the stilbene oxide was 88%.

In the previous work, the precipitates from the reactions of p-nitrobenzyl bromide and p-nitrobenzyl iodide were recrystallized from acetic acid; a dark yellow crystalline compound with mp 94-96°

Table XXVI

Products from the Reaction of p-Nitrobenzyl Halides and Hydroxide Ion in 50% Aqueous Dioxane

0.01 M p-Nitrobenzyl Halide

0.10 M NaOH

Halide	Amount of Precipitate Obtained[a]	Appearance of Precipitate	% Yield p-Nitrobenzyl Alcohol
bromide	22.9%	light yellow	66.7
bromide[b]	19.9%	white	76.5
iodide	20.8%	light yellow	76.2

[a]based on a quantitative yield of p,p'-dinitrobibenzyl ether

[b]with an oxygen atmosphere

Table XXVII

Products of the Reaction of p-Nitrobenzyl Bromide and Hydroxide Ion in 50% Aqueous Dioxane

0.01 M p-Nitrobenzyl Bromide

0.10 M NaOH

Reaction Time: 24 hr

Compound	% Yield
p,p'-dinitrobibenzyl ether	4.8
p,p'-dinitrostilbene[a]	~1.0
cis- and trans-p,p'-dinitrostilbene oxides[a]	~10.0
p-nitrobenzyl alcohol	66.7
p-nitrobenzaldehyde	trace
p-nitrotoluene	trace
p-nitrobenzyl bromide (unreacted)	trace

[a]estimated by tlc

Table XXVIII

Products of the Reaction of p-Nitrobenzyl Bromide and Hydroxide Ion in 50% Aqueous Dioxane Saturated with Oxygen

0.01 M p-Nitrobenzyl Bromide

0.10 M NaOH

Reaction Time: 24 hr

Compound	% Yield
cis- and trans-p,p'-dinitrostilbene oxides	20.0
p-nitrobenzyl alcohol	76.5
p-nitrobenzaldehyde	3.2

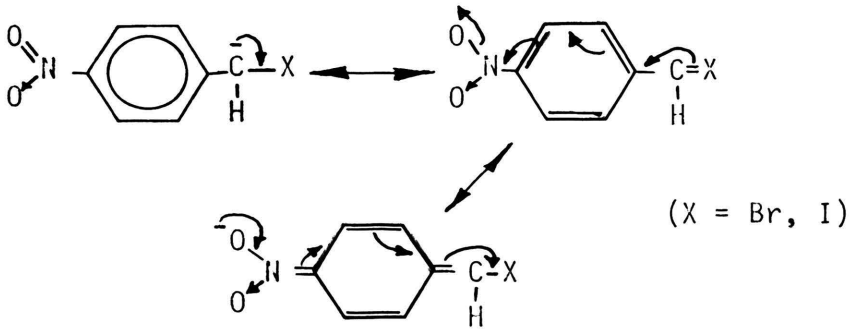
was obtained.[17] We found acetic acid to be generally unsatisfactory for recrystallization of the precipitate. Good results, however, were obtained with hexane, giving a white crystalline compound (mp 98°). The lower melting point and yellow color reported[17] are probably due to small amounts of p,p'-dinitrostilbene and other impurities that were present in the crude precipitate.

The "quantitative yield" of the bibenzyl ether reported[17] seems strange. Preferential production of the ether would necessitate a very rapid attack of the alkoxide ion on p-nitrobenzyl bromide (eq 103).

$$ArCH_2O^- + ArCH_2Br \xrightarrow{\text{rapid}} ArCH_2OCH_2Ar + Br^- \qquad (103)$$

It is claimed that this attack (eq 103) occurs much more rapidly than the hydrolysis of p-nitrobenzyl bromide (eq 10b). This seems unlikely because the concentration of hydroxide ion should be many times greater than that of the alkoxide ion.

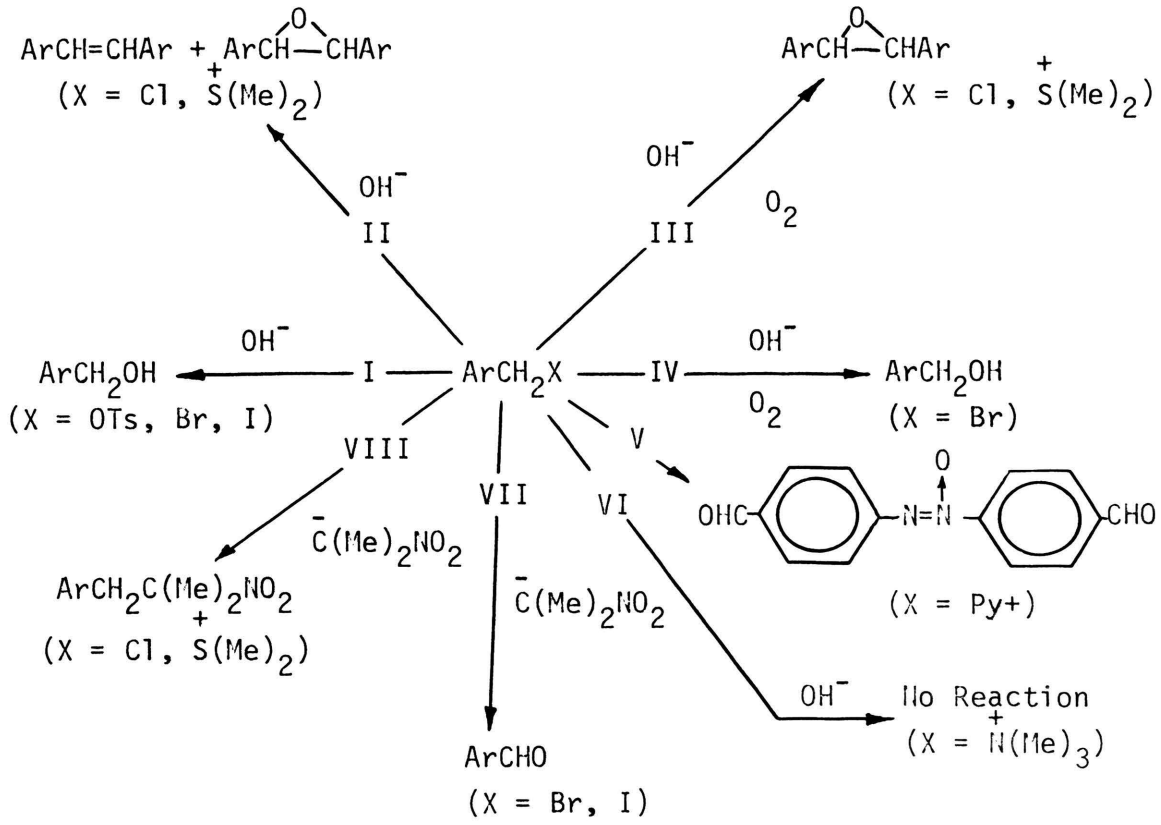
The lack of stilbene formation from p-nitrobenzyl bromide and iodide has been attributed to the inability of the halide to separate from the carbanion, presumably due to d-orbital stabilization.[17]



(X = Br, I) (104)

IV. SUMMARY

The behavior of p-nitrobenzyl compounds in basic media is unpredictable; various products are formed depending on the leaving groups and conditions. The major products obtained from several p-nitrobenzyl compounds are shown in the following diagram.



Reactions I - IV are from this work; reactions V[23], VI[22], VII[28], and VIII[28,29] are given for comparison purposes. It is seen that stilbene formation is important for cases with relatively poor

leaving groups (Cl, $\overset{+}{S}(Me)_2$); the same compounds give good yields of the C-alkylated product with 2-nitro-2-propyl anion in ethanol.[29] Both the formation of p,p'-dinitrostilbene from p-nitrobenzyl chloride and its alkylation by 2-nitro-2-propyl anion[28] are processes which are effected by p-DNB, a good electron acceptor. The behavior of o- or p-nitrobenzyl chloride in such alkylation studies[28] is unique. In contrast, "the addition of p-DNB to reactions employing benzyl chloride, m-nitrobenzyl chloride and bromide, and p-nitrobenzyl bromide and iodide is without effect on the product distribution or the rates of these reactions."[31]

The ability of nitrobenzyl compounds to form the corresponding stilbene is also paralleled by the degree to which oxygen affects the reaction products of these compounds in basic media. The reaction of p-nitrobenzyl chloride and p-nitrobenzyldimethylsulfonium salts with hydroxide ion are very sensitive to oxygen dissolved in the reaction mixture. This is contrasted by the behavior of p-nitrobenzyl bromide; its reaction with hydroxide ion is not greatly affected by oxygen. The difference may be due to the relative ease of electron transfer from the carbanion, a process which could initiate a radical chain process giving oxidation products.

$$ArCHX^- + ArCH_2X \rightarrow ArCHX^{\bullet} + ArCH_2X^{\bullet -} \qquad (105)$$

Such an electron transfer process could also serve to initiate a radical process leading to the stilbene, in the absence of oxygen.

Although electrochemical studies indicate that both p-nitrobenzyl chloride and bromide radical anions are unstable, and therefore eject readily the corresponding halide ions[30,45,46], the alkylation studies[28,29,31] strongly suggest that only p-nitrobenzyl chloride radical anion is important in these systems.

V. EXPERIMENTAL

A. Apparatus

Nuclear magnetic resonance (nmr) spectra were taken on a Varian A56-60 spectrometer; measurements were reported in δ (ppm downfield from TMS as an internal standard). Infrared spectra were taken on a Perkin-Elmer 337 grating spectrometer. Ultraviolet and visible spectra were taken on a Cary-14 spectrometer. Chlorine kinetic isotope effects were measured on an Atlas MAT 150 mass spectrometer. The gain of the "B" amplifier was changed by the substitution of a Victoreen 10^{11} ohm resister for the original 10^{10} ohm resistor, giving it the same gain as the "A" amplifier. Gas liquid chromatography (glc) analysis was carried out on a Varian Aerograph 600-D gas chromatograph with a flame ionization detector, except where otherwise noted. The column was a 6 ft x 0.125 in 5% SE-30 on 60-80 mesh Chromosorb B. The mass spectra were taken on a duPont model 491 mass spectrometer. Melting points are uncorrected.

B. Chemicals

p-Dioxane (Matheson reagent grade) was passed through a column of basic alumina to remove peroxides,[67] refluxed for 12 hr over sodium metal, followed by distillation through a 2-ft column packed with glass helices. Only the middle fraction was used for kinetic studies; bp 101° (lit[68] bp 101° [750]).

p-Nitrobenzyl chloride (Eastman) was recrystallized twice from hexane; mp 71° (lit[68] mp 71°).

p-Nitrobenzyl bromide (Matheson) was recrystallized three times from hexane; mp 99° (lit[68] mp 99-100°).

p-Nitrobenzyl alcohol (Aldrich) was recrystallized from hot water, and then from benzene; mp 96° (lit[68] mp 96-97°).

p-Nitrobenzaldehyde (Matheson) was recrystallized from ethanol; mp 106° (lit[68] mp 106°).

p-Dinitrobenzene (Eastman) was passed through a column of basic alumina, using benzene as the solvent. The solution obtained was concentrated, and the p-dinitrobenzene was recrystallized from it; mp 172° (lit[68] mp 173-174°).

p-Nitrotoluene (Eastman) was recrystallized from hexane; mp 52° (lit[68] mp 54.5°).

p-Nitrobenzyldimethylsulfonium p-toluenesulfonate (tosylate) was prepared by the reactions of p-nitrobenzyl p-toluenesulfonate with dimethyl sulfide in acetonitrile at room temperature.[12] The salt, dissolved in methanol, was precipitated by addition of ether. The salt, dissolved in methanol, was precipitated by addition of ether. The salt was recrystallized this way a total of three times; mp 137-138° (lit[12] mp 138.5-139.2°).

p-Nitrobenzyldimethylsulfonium bromide was prepared by the reaction of excess dimethylsulfide with p-nitrobenzyl bromide at room temperature for 24 hr.[69] The salt was washed with ether, dissolved in methanol, and precipitated with ether. The dissolution and precipitation was repeated; mp 111-112° (lit[69] mp 112-113°).

trans-p,p'-Dinitrostilbene was prepared by the method of Walden and Kernbaum.[4] It was recrystallized from aqueous dimethyl

sulfoxide followed by two recrystallizations from acetone; mp 300-301° with sublimation (lit[68] mp 288 to 305°). The visible and ultraviolet spectra in DMF has λ_{max} = 368 nm with log ε = 4.568 (lit[63] λ_{max} = 368 nm, log ε = 4.577).

cis-p,p'-Dinitrostilbene was prepared by the photochemical isomerization of the trans isomer in benzene, followed by column chromatography on neutral alumina with benzene.[63] The cis isomer was recrystallized from benzene; mp 187° (lit[63] mp 187°). The visible and ultraviolet spectra in DMF showed λ_{max} = 320 nm with log ε = 4.199 (lit[63] λ_{max} = 320 and log ε = 4.193).

cis- and trans-p,p'-Dinitrostilbene oxides were prepared by the method of Bergmann and Hervey.[6] The two isomers were separated by fractional recrystallization from dioxane-water.[34] The trans isomer was further recrystallized from ethyl acetate; mp 201° (lit[34] mp = 201°). Nmr analysis showed aromatic protons at δ = 8.12 ppm and a singlet at δ = 4.38 ppm with relative areas of 4 : 1. The ultraviolet spectrum in DMF showed λ_{max} = 291 nm and log ε = 4.371. The cis isomer was recrystallized from acetic acid; a yellowish solid with mp 153° was obtained. The tlc showed impurities, primarily p,p'-dinitrostilbene, and a small amount of trans-p,p'-dinitrostilbene oxide. The sample was further purified by preparative tlc on silica gel plates, developed in benzene. A white solid, free of impurities, was obtained; mp 165° (lit[34] mp 165°). The mass spectrum of the compound gave a molecular weight of 286. The nmr showed aromatic protons at δ = 7.93 ppm and a singlet at δ = 4.79 ppm, with relative

areas of 4 : 1. The ultraviolet spectrum in DMF showed λ_{max} = 277 nm with log ε = 4.264.

p,p'-Dinitrobibenzyl was prepared by the reaction of p-nitrotoluene with potassium t-butoxide in t-butyl alcohol.[44] The product was recrystallized from benzene; mp 181° (lit[68] mp 180.5°).

p-Nitrobenzyl iodide was prepared by the Finkelstein reaction.[70] p-Nitrobenzyl chloride was dissolved in aqueous acetone containing dissolved excess sodium iodide. The p-nitrobenzyl iodide which precipitated was recrystallized twice from acetone; mp = 124° (lit[70] mp = 124°). p-Nitrobenzyl p-toluenesulfonate (tosylate) was prepared by the reaction of tosyl chloride with p-nitrobenzyl alcohol in dry pyridine at -10°.[71,72] The resulting ester was recrystallized from a mixture of isopropyl alochol-petroleum ether;[73] mp = 103° (lit[72] mp = 103-104°).

Di-t-butyl nitroxide was prepared by the method of Hoffman,[74] with the exception of replacing the morton flask and high-speed stirrer with an ordinary round-bottom flask and teflon-paddled true-bore stirrer; the yield was 10%. Glc (SE-30 at 80°) indicated the presence of impurities; they were removed by fractional freezing from a solution of pentane at Dry ice--acetone temperature. The sample had identical glc behavior as a commercially available sample (Eastman) of di-t-butyl nitroxide.

p,p'-Dinitrotolane was prepared by the method of Ruggi and Lang.[75] trans-p,p'-Dinitrostilbene was converted to the dibromide by reaction with bromine in boiling nitrobenzene under strong

illumination with a Hanovia lamp. The dibromide was then treated with alcoholic KOH; the crude material was dissolved in a minimum amount of hot glacial acetic acid. The solution gave a small amount of crystalline material on cooling. The filtrate was concentrated to dryness, followed by recrystallization from ethanol; mp 212-214° (lit[75] mp 210-212°). The tlc of the resulting tolane showed it to be pure except for a very small amount of p,p'-dinitrostilbene.

p,p'-Dinitrobibenzyl ether was obtained from the reaction of p-nitrobenzyl bromide and sodium hydroxide in aqueous dioxane.[17] The precipitate, obtained from the neutralized reaction mixture, was recrystallized from hexane; a white crystalline compound with mp 98° (lit[76] mp 97-98° from ethanol or benzene (almost colorless crystals) was obtained. The nmr showed aromatic protons at δ = 7.97 ppm and a singlet at δ = 4.93 ppm, with relative areas of 2 : 1. The infrared showed two broad peaks at 1120 cm^{-1} and 1097 cm^{-1} which are characteristic for aliphatic ethers. The mass spectrum gave a molecular weight of 288.

C. Labeled Compounds

α,α-d_2-p-Nitrobenzyl Chloride. To a solution of 13.3 g (0.10 mol) of anhydrous aluminum chloride in 50 ml of anhydrous ether, was added 4.2 g (0.10 mol) of lithium aluminum deuteride at ice-bath temperature.[77] After stirring for one-half hour at room temperature, a solution of 7.8 g (0.041 mol) of p-nitrobenzoic acid ethyl ester in about 250 ml of anhydrous ether was added dropwise over a period of 1 hr. The reaction mixture was hydrolyzed after two hours by

dropwise addition of water, followed by dilute sulfuric acid. Extraction, drying, and removal of the solvent, followed by recrystallization from hot water gave 3.2 g of a white solid (52% yield) with mp 93°. Ir and nmr were consistent with α,α-d_2-p-nitrobenzyl alcohol. A solution of 2.8 g (0.023 mol) of thionyl chloride in 50 ml of chloroform was slowly added to the sample of the alcohol dissolved in 100 ml of chloroform. The solution was stirred for 12 hr refluxed for an additional 2 hr. Removal of the chloroform left a solid and excess thionyl chloride. The solid was recrystallized from hexane, and further purified by column chromatography on neutral alumina with cyclohexane as the solvent. The fractions containing p-nitrobenzyl chloride were combined, concentrated, and cooled. The resulting crystalline compound (mp 71°) was shown to be free of thionyl chloride and p-nitrobenzyl alcohol by glc. Nmr showed the side chain to be completely deuterated (> 99% D). A sample of ordinary p-nitrobenzyl chloride was prepared by the same procedure from p-nitrobenzyl alcohol from comparative rate studies.

α-d_1-p-Nitrobenzyl Chloride. To a solution of 6.7 g (0.05 mol) of anhydrous aluminum chloride in 25 ml of anhydrous ether was added 2.1 g (0.05 mol) of lithium aluminum deuteride at ice-bath temperature.[77] After stirring for one-half hour at room temperature, a solution of 7.6 g (0.05 mol) of p-nitrobenzaldehyde in 200 ml of anhydrous ether was added dropwise over a one-hour period. Five minutes after the last addition of the aldehyde, the reaction mixture

was hydrolyzed. The reaction mixture worked up in the same manner as described for α,α-d_2-p-nitrobenzyl alcohol; 5.1 g of a white solid, mp 93° (66% yield) was obtained. The infrared and nmr spectra were consistent with α-d_1-p-nitrobenzyl alcohol.

The alcohol was converted to the corresponding chloride in the manner described previously. The resulting chloride (mp 70-71°) was shown to be free of thionyl chloride and p-nitrobenzyl alcohol by glc. Nmr showed aromatic protons δ = 7.98 ppm, and benzylic protons δ = 4.71 ppm, with relative areas of 4 : 1.2.

D. Experimental Procedures

Kinetic Studies. The rate of the reaction of p-nitrobenzyl chloride with hydroxide ion was followed by an electrometic titration of the chloride ion released, using the method previously described.[9] Fifty percent aqueous dioxane (v/v) refers to a mixture of equal volumes of dioxane and water. Kinetic runs were conducted at 25.00 ± 0.02° in flasks blackened to exclude light, except as otherwise noted. All solutions were prepared from freshly distilled dioxane; reproducible results could not be obtained from old solutions.

Product Analyses. In the majority of reactions studied, precipitates appeared as the reaction progressed. Additional precipitation of reaction products was usually accomplished by neutralization of the reaction mixtures, dilution with water, and storing in a refrigerator. The total precipitates were isolated by filtration, washed with water, and dried. The filtrates were extracted with chloroform of methylene chloride, the organic layer dried

(Na_2SO_4), and the solvent completely removed. The resulting residues were analyzed by glc (see Appendix B).

The yields given in tables were the analyses of both the precipitate and the residue obtained by extraction of the filtrate, unless otherwise noted.

E. Experiments

Exchange Studies. The reaction mixture of 0.01 M α,α-d_2-p-nitrobenzyl chloride and 0.10 M NaOH in 50% aqueous dioxane at 25°, was quenched with dilute sulfuric acid after 42% reaction. The precipitate was removed by filtration; the filtrate was extracted (3 x 25 ml) with chloroform, and the chloroform layer dried (Na_2SO_4). The solvent was completely removed on a rotary evaporator; the resulting solid was redissolved in the minimum amount of cyclohexane, and chromatogrammed on a column of neutral alumina with cyclohexane as the solvent. The fractions containing nitrobenzyl chloride were combined, concentrated, and cooled; pure p-nitrobenzyl chloride was recovered. Nmr analysis of the recovered p-nitrobenzyl chloride showed aromatic protons δ = 7.98 ppm, and benzylic protons δ = 4.71 ppm with relative areas of 8 : 1.

A similar experiment with added p-nitrobenzaldehyde (0.01 M) was interrupted by quenching with dilute sulfuric acid after 50% reaction. The chloroform extract was washed with dilute $NaHSO_3$ to remove unreacted p-nitrobenzaldehyde, and then treated in a manner identical to the first experiment. The recovered p-nitrobenzyl chloride showed only aromatic protons δ = 7.98 ppm, and no benzylic protons.

Deuterium Isotope Effects. The deuterium isotope effect for the p-nitrobenzyl chloride--p,p'-dinitrostilbene transformation was determined by two concurrent kinetic runs: one with α,α-$\underline{d}_2$-p-nitrobenzyl chloride, and the other with the sample of p-nitrobenzyl chloride prepared by the same synthetic route as the labeled compound. To a solution of 45 ml of dioxane and 50 ml of 0.2 M NaOH at 25°, was added 5 ml of a 0.2 M solution of p-nitrobenzyl chloride in dioxane at 25°; the solutions were mixed and the flasked stoppered. The second run was started in an identical manner except that 5 ml of a 0.2 M solution of α,α-$\underline{d}_2$-p-nitrobenzyl chloride in dioxane was used. The rates of the two reactions are followed by periodically removing 5 ml aliquots for analysis of the chloride ion released; the rate data are given in Tables II and III, p 32.

A second experiment was performed to determine the kinetic isotope effect for the reaction with added p-nitrobenzaldehyde. The kinetic runs were carried out in the same manner as previously described, except that the p-nitrobenzyl chloride solutions were added to a solution of 40 ml of dioxane and 50 ml of a 0.2 M NaOH solution containing 5 ml of a 0.2 M solution of p-nitrobenzaldehyde in dioxane. The rate data are given in Tables IV and V, p 34.

A third experiment involved the reaction of p-nitrobenzyl chloride and hydroxide ion, using only partially deuterated p-nitrobenzyl chloride. The reactions were initiated by the addition of 25 ml of a 0.2 M p-nitrobenzyl chloride solution in dioxane to a solution of 25 ml of dioxane and 50 ml of a 0.1 M NaOH; the rate data are given in Tables VI and VII, p 35.

Chlorine Kinetic Isotope Effects. The product sample was prepared as follows: 50 ml of a 0.2 M p-nitrobenzyl chloride solution in dioxane was added to a solution of 450 ml of dioxane and 500 ml of 0.2 M NaOH at 25°. The reaction mixture was quenched after 10% reaction by addition of 100 ml of 1 M nitric acid. The reaction mixture was extracted (3 x 100 ml) with ether to remove unreacted p-nitrobenzyl chloride and other organic material. The pH was adjusted to a value of 6, and sufficient KNO_3 was added to make the ionic strength approximately equivalent to that of a 0.4 M KNO_3 solution.[38] The chloride ion was then precipitated by the addition of a 10% excess of silver nitrate to the hot stirred solution. The completeness of precipitation was checked after the silver chloride had coagulated. The silver chloride was then collected by filtration, washed with a solution of 2 ml of nitric acid in a liter of distilled water; the precipitate was dried for 8 hr at a temperature of 110°.

The reactant sample was prepared in a similar manner, except on a smaller scale; 5 ml of a 0.2 M p-nitrobenzyl chloride solution in dioxane was added to a solution of 45 ml of dioxane and 50 ml of 0.2 M NaOH. The mixture was allowed to react for more than 10 half-lives. The organic precipitate that had formed was removed by filtration, and the filtrate acidified by the addition of dilute nitric acid. The extraction and precipitation were carried out in a manner similar to that of the product sample. The silver chloride precipitates were then converted to methyl chloride for analysis.

The mass spectrometer required a gas pressure from 50 to 100 torr. Therefore, the amount of methyl chloride required for 0.25 liter sample flasks is given by:

$$n = \frac{(0.10 \text{ atm})\ (0.25 \text{ l})}{(0.082 \text{ l atm/mole } ^\circ\text{K})\ (298 \ ^\circ\text{K})} \qquad (106)$$

$$n = 1 \times 10^{-3} \text{ moles}$$

Therefore, 0.144 grams (1 mmol) of silver chloride was used; the silver chloride was placed in a reaction flask fitted with a break-off tip on one end, and a 10/30 inner joint at the other end. A 100% excess of methyl iodide was added,[39] using a microliter syringe; the contents were frozen with liquid nitrogen, and the flask evacuated and sealed under vacuum. The contents of the flask were allowed to react at 120° for 48 hr.

The flask was then attached to a vacuum line by means of a 10/30 outer joint containing a glass encapsulated nail. The vacuum manifold was then evacuated, and then closed off from the pumping system. The reaction flask containing the methyl chloride was then opened by dropping the mail on the break-off tip. The contents of the flask were then vacuum transferred to a flask containing powdered KOH (to remove any HCl gas). The methyl chloride was then vacuum transferred to a sample flask fitted with a stopcock and 10/30 joint. In this second transfer, unreacted methyl iodide was removed; methyl iodide is a solid at dry-ice temperatures, and methyl chloride is a gas. The impure gas sample (frozen with liquid nitrogen) was allowed to

warm to the temperature of a Dry-ice acetone bath; the methyl chloride escaped into the manifold, leaving unreacted methyl iodide. The methyl chloride was then frozen (with liquid nitrogen) into the sample flask for analysis on the mass spectrometer.

Samples were introduced into the sample chambers of the mass spectrometer at approximately the same pressure, by using a manifold fitted with a mercury leveling bulb to adjust the pressure of the gas samples. Small variations of pressure were then adjusted using the variable pressure adjustment on the instrument. The isotopic ratios of each sample, R_{37}/R_{35} and P_{37}/P_{35}, were then determined. The 52 mass peak (CH_3Cl^{37}) was focused on the small plate, which is connected to the "A" amplifier. The other mass peaks therefore fall on the large plate, which is connected to the "B" amplifier (with gain increased to that of the "A" amplifier by changing the 10^{10}-ohm resistor to 10^{11} ohms). The currents from the "A" and "B" amplifiers were then made equal by means of the voltage divider; the ratios then were read from the voltage divider.*

Effect of Light on Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion. The reaction vessels used were 24/40 long neck pyrex flasks; one flask was rendered opaque with black paint. The source of illumination was a 140 watt Hanovia lamp at a distance of 6 inches. In each flask, 45 ml of dioxane and 50 ml of 0.2 M NaOH were added. The flasks were placed in the water bath, and the illumination begun just before the reaction was iniatiated by the addition of

*A complete description, and sample calculations are given in the instruction manual that comes with the instrument.

5 ml of a 0.2 M p-nitrobenzyl chloride solution in dioxane. The rate data are given in Tables VIII and IX, p 40.

Effect of Oxygen on the Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion. p-Nitrobenzyl chloride, 0.343 g (2 mmol), was dissolved in 50 ml of dioxane, and added to a 500 ml 3-neck flask fitted with a fritted bubbler, and a water trap to allow gases to escape. A slow stream of oxygen was passed through the magnetically stirred solution for a few minutes, followed by addition of 50 ml of 0.2 M NaOH; the flow of oxygen was continued for 15 min after the reaction was initiated. A small sample was withdrawn for glc analysis after 12 hr; p-nitrobenzaldehyde, along with smaller amounts of p-nitrobenzyl alcohol and p-nitrobenzyl chloride were shown to be present. The reaction mixture contained a small amount of a white precipitate after 36 hr; the color of the solution was light pink. Neutralization of the reaction mixture with dilute HCl caused the color to disappear. The reaction mixture was diluted with an equal volume of water, and stored for 12 hr in a refrigerator. The precipitate was isolated by filtration, washed with water, and dried. The resulting white precipitate (0.2460 g) was analyzed by tlc, and shown to be exclusively a mixture of cis- and trans-p,p'-dinitrostilbene oxides (88% yield) and no p,p'-dinitrostilbene. Nmr analysis of the precipitate gave a singlet at δ = 4.38 ppm, and one at δ = 4.79 ppm, with relative areas of 1 : 1.57. This corresponds to 42% trans- and 58% cis-p,p'-dinitrostilbene oxide. The aromatic region was complex, and was centered at approximately δ = 8.04 ppm.

The precipitate was fractionally recrystallized from dioxane--water; the two isomers obtained were shown to be identical to authentic samples by undepressed mixture-melting points. The ultraviolet spectrum of the precipitate gave λ_{max} = 284 nm and log ε = 4.296 (DMF).

The filtrate was extracted (3 x 50 ml) with methylene chloride, the organic layer dried (Na_2SO_4), and the solvent removed completely on a rotary evaporator. The solid residue (0.0390 g) was analyzed by glc, and shown to contain 40.8% p-nitrobenzyl alcohol (0.0159 g; 5.2% yield), and 15.4% p-nitrobenzaldehyde (0.0006 g; 2.0% yield). Tlc analysis (95% chloroform--5% ethanol) showed three spots: a major spot with the same R_f value as p-nitrobenzyl alcohol, a small spot with the same R_f value as p-nitrobenzaldehyde, and a small spot with the same R_f value as p-nitrobenzoic acid. The latter spot gave an acidic reaction with Lacmoid indicator (pH range 4.4 - 6.2). It was estimated to correspond to about 4% yield based on comparison of spot size of samples of known weight. The complete analysis is given in Table X, p 44.

The kinetics of the reaction with oxygen was determined in the same manner as described previously except that the reaction mixture had a slow stream of oxygen passing through it. Tank oxygen was passed through a scrubber filled with a 50% aqueous dioxane mixture before passing into the reaction mixture. The rate data are given in Tables XI and XII, p 45.

Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in the Absence of Oxygen. The dioxane used in this case was purified as explained previously, followed by an additional distillation from

lithium aluminum hydride. The dioxane and sodium hydroxide solutions were swept with argon for 1/2 hr before being placed in the reaction vessel. An all glass vessel (see Figure 6) consisting of two flasks with side arms for addition of solutions was used; the vessel was fitted with a vacuum stopcock and O ring seal for attachment to the vacuum line. In one flask, 50 ml of 0.2 M NaOH was placed. In the other flask, 40 ml of dioxane and 10 ml of a 0.1 M solution of p-nitrobenzyl chloride in dioxane were pipetted. The apparatus was attached to a vacuum line, flushed with argon, and the openings in the side arms closed with a torch. The solutions were degassed by five freeze--thaw cycles: freezing with liquid nitrogen, evacuation, and thawing accompanied by stirring. After closing the vacuum stopcock, and removing the apparatus from the vacuum line, the two solutions were mixed under vacuum (the partial pressure of the solvent) by shaking the apparatus. After 24 hr, the contents were neutralized with dilute HCl, diluted with an equal volume of water, and cooled for 24 hr. The precipitate was isolated by filtration, washed, and dried at 50° and 2 torr for 4 hr; the precipitate weighed 0.1320 g. The visible and ultraviolet spectra showed two bands: λ_{max} = 360 nm, and λ_{max} = 284 nm (DMF). The tlc of the precipitate is shown in Table XXIX. A small spot, with an R_f value of 0.58, was always observed in the precipitates from p-nitrobenzyl chloride if the dinitrostilbene is present. A small sample of the compound was isolated from the precipitate by preparative tlc; it was shown to have a molecular weight of 268 by mass spectroscopy.

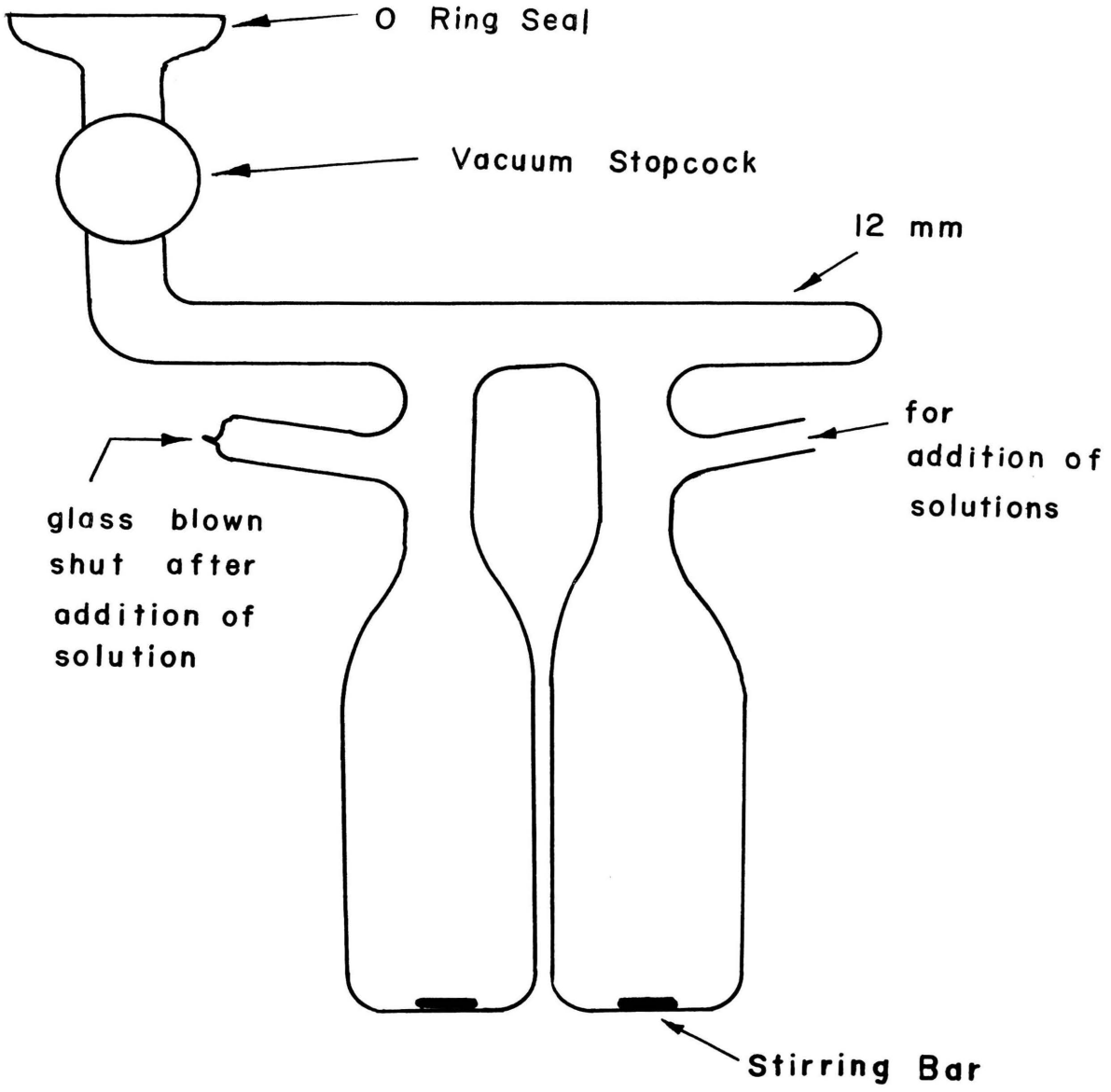


Figure 6. Apparatus used for studying reactions using degassed solutions

Table XXIX

Thin Layer Chromatograph of Precipitate from Reaction of p-Nitrobenzyl Chloride in the Absence of Oxygen

R_f Value	Estimated Amount**
0.00	trace
0.03	small
0.21	trace
0.28	large
0.39	large
0.47*	major
0.58	small

Comparison of Standard Compounds

R_f Value	Compound
0.28	cis-p,p'-dinitrostilbene oxide
0.39	trans-p,p'-dinitrostilbene oxide
0.48*	cis- and trans-p,p'-dinitrostilbene
0.58	p,p'-dinitrotolane

*Gave a yellow fluorescence with a long wave U.V. Lamp (366 nm)

**major > large > significant > small > trace

The compound in question has the same R_f value as a sample of authentic p,p'-dinitrostilbene.

The filtrate was extracted (3 x 50 ml) with chloroform. The organic layer was dried (Na_2SO_4), and the solvent completely removed. The residue (0.0055 g) was analyzed by glc and shown to be 89% p-nitrobenzyl alcohol (0.0049 g; 3.2% yield), 3.6% p-nitrobenzaldehyde (0.0002 g; 0.1% yield), and a trace of p-nitrotoluene. The complete analysis is given in Table XIII, p 46.

Effect of p-Dinitrobenzene on the Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion. A solution of 100 ml of 0.2 M NaOH and 50 ml of dioxane was placed in a flask fitted with a side arm containing a solution of 0.1720 g (0.001 mol) of p-nitrobenzyl chloride and 0.1680 g (0.001 mol) of p-dinitrobenzene in 50 ml of dioxane. The flask was attached to a vacuum line, and the contents were degassed with three freeze-thaw cycles. The reaction was initiated by rotating the side arm, allowing the contents to mix.

After 24 hr, the reaction mixture was worked up as previously described; the weight of the precipitate was 0.1136 g. The tlc of the precipitate is given in Table XXX, p 118.

The filtrate was extracted (3 x 50 ml) with methylene chloride; the organic layer was dried (Na_2SO_4), and the solvent completely removed. The resulting residue, 0.1820 g, was analyzed by glc at 170°, and found to be 56.8% p-dinitrobenzene (0.1030 g; 61.3% recovered), 5.5% p-nitrotoluene (0.0100 g; 7.7% yield), 1.3% p-nitrobenzaldehyde (0.0016 g; 1.3% yield), and 15.7% p-nitrobenzyl alcohol (0.0286 g; 18.9% yield).

Table XXX

Thin Layer Chromatograph of the Precipitate from the Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion in the Presence of Added p-Dinitrobenzene

R_f Value	Estimated Amount**
0.00	trace
0.04	small
0.15	small
0.28	large
0.32*	trace
0.39	large
0.45	significant
0.48*	significant
0.57	major

Comparison of Standard Compounds

R_f Value	Compound
0.28	cis-p,p'-dinitrostilbene oxide
0.39	trans-p,p'-dinitrostilbene oxide
0.45	p,p'-dinitrobibenzyl
0.48*	cis- and trans-p,p'-dinitrostilbene
0.57	p-dinitrobenzene
0.58	p,p'-dinitrotolane

*Gave a yellow fluorescence with a long wave U.V. lamp (366 nm)

**major > large > significant > small > trace

Glc analysis at 270° of the precipitate gave 7.1% cis-p,p'-dinitrostilbene (0.0080 g; 6.0% yield), 10.5% p,p'-dinitrobibenzyl (0.0119 g; 8.8% yield), 22.0% cis- and trans-p,p'-dinitrostilbene oxides (0.0250 g; 17.5% yield), and 12.4% trans-p,p'-dinitrostilbene (0.0141 g; 10.4% yield). Only about 1% recovered p-dinitrobenzene was detected in the precipitate. An estimate of the amount of trans-p,p'-dinitrostilbene was made from the absorbance of a DMF solution of the precipitate at 368 nm; the value, 13% (0.0140 g; 11.0% yield) was in good agreement with the value obtained by glc. The complete analysis is given in Table XVII, p 57.

Effect of Di-t-butyl Nitroxide on the Reaction of p-Nitrobenzyl Chloride and Hydroxide Ion. The initial investigation involved a series of reactions to see how the products were affected with various amounts of the nitroxide. The di-t-butyl nitroxide was weighed in the reaction flasks, and to each flask, 95 ml of the reaction medium were added. (The reaction medium was prepared by mixing 450 ml of dioxane with 500 ml of 0.2 M NaOH, and sweeping the mixture with nitrogen for one-half hour). The reaction was initiated by the addition of 5 ml of 0.2 M solution of p-nitrobenzyl chloride in dioxane. The flasks were stoppered, and the contents mixed by swirling. The reaction mixtures were neutralized with dilute hydrochloric acid after a 24 hr reaction period, and worked up in the usual manner. The tlc of the precipitates is shown in Figure 7. The results of the preliminary analysis are given in Table XVIII, p 65.

In order to make a valid comparison to the results of the reaction of p-nitrobenzyl chloride and hydroxide in the absence of

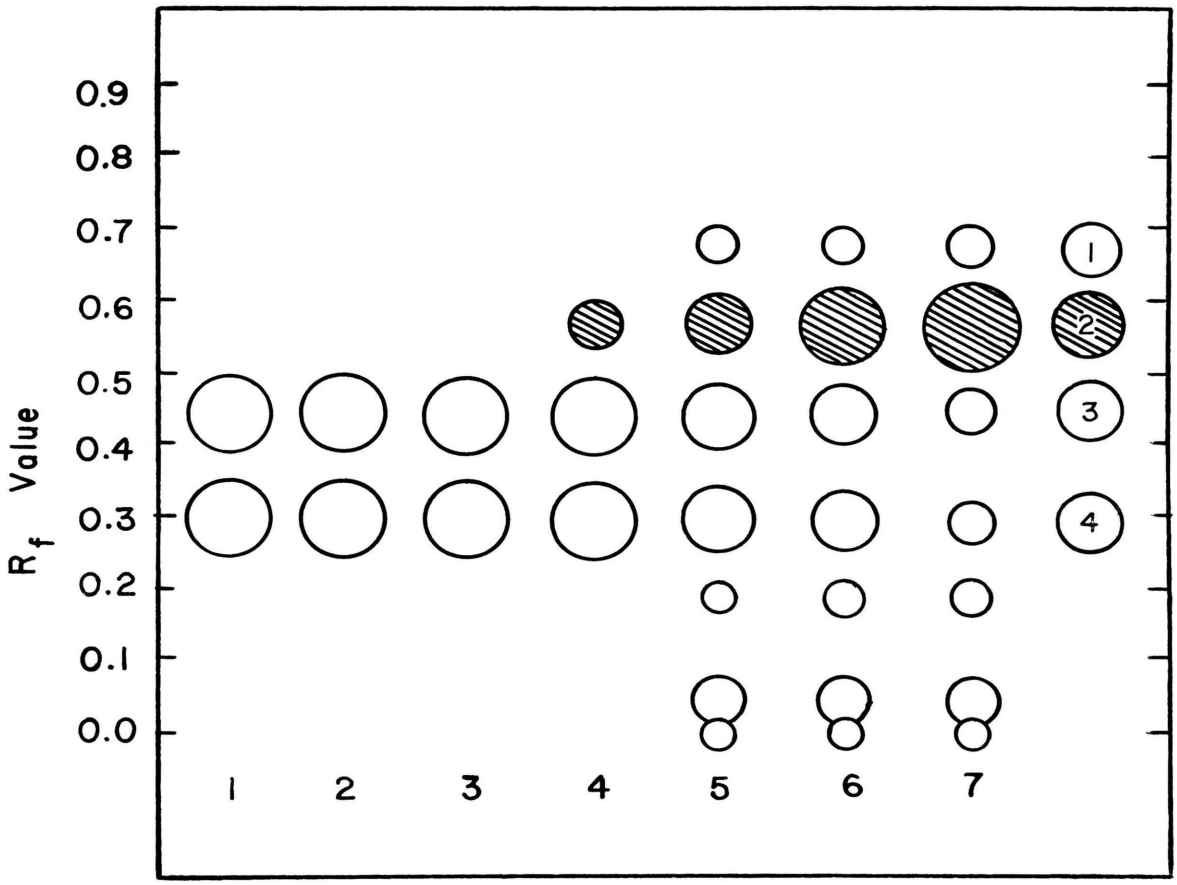


Figure 7. Thin Layer Chromatograph of Precipitates in Table XVIII

Molarity of Nitroxide

1 = 0.010 M

2 = 0.005 M

3 = 0.004 M

4 = 0.003 M

5 = 0.002 M

6 = 0.001 M

7 = no nitroxide

Standard Compounds

1 = p,p'-dinitrotolane

2 = p,p'-dinitrostilbene

3 = trans-p,p'-dinitrostilbene oxide

4 = cis-p,p'-dinitrostilbene oxide

appears as a yellow fluorescent spot with a long wave U.V. lamp (366 nm)

oxygen (Table XIII), two of the experiments with the nitroxide were repeated using conditions identical (the same dioxane, sodium hydroxide, and p-nitrobenzyl chloride solutions) to those of the degassed case.

In the first experiment, 0.015 g (0.0001 mol) of di-t-butyl nitroxide was used. The nitroxide was dissolved in 40 ml of dioxane and added to a flask (see Figure 6) containing 10 ml of a 0.1 M solution of p-nitrobenzyl chloride in dioxane. To the second flask was added 50 ml of 0.2 M NaOH. The solutions were degassed in the manner previously described, using five freeze--thaw cycles. The precipitate obtained weighed 0.1041 g. An oily residue (0.0475 g) was obtained by concentrating the chloroform extract of the filtrate. Glc of the residue showed that it was 38.5% p-nitrobenzyl alcohol (0.0182 g; 11.9% yield), 4.5% p-nitrobenzaldehyde (0.0021 g; 1.4% yield), and a trace of p-nitrotoluene; the rest of the material was unaccounted for. The complete analysis is given in Table XIX, p 66.

In the second experiment, 0.080 g (0.0055 mol) of the nitroxide was added; the precipitate obtained weighed 0.0491 g. The ultraviolet spectrum of the precipitate gave λ_{max} = 284 nm and log ε = 4.290 (DMF). The oily residue (0.1824 g) was shown to contain 41.0% p-nitrobenzyl alcohol (0.0747 g; 49.0% yield), 4.9% p-nitrobenzaldehyde (0.0089 g; 5.9% yield), 8.7% unreacted p-nitrobenzyl chloride (0.159 g; 9.3% recovered), and traces of p-nitrotoluene and di-t-butyl nitroxide. Small amounts of unidentified compounds were also present. The complete analysis is given in Table XX, p 67.

The Reaction of p-Nitrobenzyl Chloride with p-Nitrobenzaldehyde and Hydroxide Ion in the Presence of Di-t-butyl Nitroxide. p-Nitrobenzaldehyde, 0.1580 g (~0.0010 mol), and 0.114 g (0.0010 mol) of di-t-nitroxide were added to 45 ml of dioxane, followed by the addition of 50 ml of 0.2 M NaOH. To the mixture was added 50 ml of a 0.2 M solution of p-nitrobenzyl chloride in dioxane (0.0010 mol of p-nitrobenzyl chloride).

A second sample was prepared without the nitroxide, using 0.1571 g (~0.0010 mol) of p-nitrobenzaldehyde. The two samples were allowed to react for 24 hr; the reaction mixtures were worked up as previously described. The precipitates obtained weighed 0.2469 g and 0.2493 g, respectively; the tlc of the two precipitates is given in Table XXXI, p 123.

Reaction of p-Nitrobenzyldimethylsulfonium Tosylate and Hydroxide Ion. p-Nitrobenzyldimethylsulfonium tosylate, 0.3691 g (0.0010 mol), was dissolved in 50 ml of distilled water, and heated to 60°. Upon addition of 50 ml of 0.2 M NaOH solution at 60°, a red color developed instantly. After 1 min, a significant amount of precipitate had formed, and the color of the solution had faded; the reaction mixture smelled strongly of dimethyl sulfide. After 4 hr at 60°, the reaction mixture was neutralized with dilute HCl. The precipitate was isolated by filtration, washed with distilled water, and dried at 50° and 2 torr for 2 hr; 0.1369 g of a yellow precipitate was obtained. Tlc analysis of the precipitate showed two major spots with the same R_f values as p,p'-dinitrostilbene and trans-p,p'-dinitrostilbene oxide, and a trace spot

Table XXXI

Thin Layer Chromatograph of Precipitates from the Reaction of p-Nitrobenzyl Chloride and p-Nitrobenzaldehyde with Hydroxide Ion, With and Without Added Di-t-butyl Nitroxide

With Added Di-t-butyl Nitroxide	
R_f Value	Estimated Amount**
0.30	major
0.45	major

Without Added Di-t-butyl Nitroxide	
R_f Value	Estimated Amount**
0.00	small
0.30	major
0.45	major
0.59*	trace

Comparison of Standard Compounds	
R_f Value	Compound
0.30	cis-p,p'-dinitrostilbene oxide
0.44	trans-p,p'-dinitrostilbene oxide
0.57*	cis- and trans-p,p'-dinitrostilbene

*Gave a yellow fluorescence with a long wave U.V. Lamp (366 nm)

**major > large > significant > small > trace

with the same R_f value as cis-p,p'-dinitrostilbene oxide. The visible and ultraviolet spectra showed two bands: λ_{max} = 368 nm, and λ_{max} = 290 nm (DMF). Analysis of the precipitate is given in Table XXIII, p 81.

Effect of Oxygen on the Reaction of p-Nitrobenzyldimethylsulfonium Tosylate and Hydroxide Ion. p-Nitrobenzyldimethylsulfonium tosylate, 0.3664 g (0.0010 mol) was dissolved in 50 ml of distilled water at 60°, and a stream of oxygen passed through the stirred solution for 15 min. Upon addition of 50 ml of 0.2 M NaOH solution at 60°, a red color developed instantly; the color quickly faded, giving a yellow solution and a precipitate. The solution was neutralized with dilute HCl after 4 hr; the reaction mixture was treated as described in the previous case. A yellow precipitate, 0.0826 g, was obtained; the tlc of the precipitate showed two components: a major component with the same R_f value as trans-p,p'-dinitrostilbene oxide, and a trace spot for the minor component, which had the same R_f value as p,p'-dinitrostilbene. The visible and ultraviolet absorption spectra showed two bands: λ_{max} = 290 nm, with a shoulder at 368 nm (DMF). The analysis of the precipitate is given in Table XXIII, p 81.

The filtrate was extracted with chloroform (3 x 50 ml), the organic layer dried (Na_2SO_4), and the solvent completely removed. The residue, 0.0426 g, was shown by glc to be 11.8% p-nitrobenzaldehyde (0.0050 g; 3.4% yield), and 38.8% p-nitrobenzyl alcohol (0.0165 g; 11.0% yield).

Effect of Di-t-butyl Nitroxide on the Reaction of p-Nitrobenzyldimethylsulfonium Tosylate and Hydroxide Ion. p-Nitrobenzyldimethylsulfonium tosylate, 0.3665 g (0.0010 mol), and 0.0846 (0.0006 mol) of di-t-butyl nitroxide were added to 50 ml of distilled water at 60°; the nitroxide only partially dissolved. The mixture was added to 50 ml of 0.2 M NaOH at 60°. A red color developed instantly; the color presisted for a long time, relative to the experiment with no nitroxide. Only a small amount of a light colored precipitate had formed after 1 hr.

After 4 hr at 60°, the reaction mixture was neutralized with dilute HCl, and the reaction mixture was worked up as previously described. The resulting yellowish precipitate (0.1328 g) showed two components by tlc: a major component with the same R_f value as trans-p,p'-dinitrostilbene oxide, and a minor component with the same R_f value as p,p'-dinitrostilbene. The visible and ultraviolet spectra showed a band with λ_{max} = 290 nm, with a shoulder at 368 nm (DMF). The analysis of the precipitate is given in Table XXIII, p 81.

Reaction of p-Nitrobenzyldimethylsulfonium Bromide and Hydroxide Ion. The reaction of p-nitrobenzyldimethylsulfonium bromide and hydroxide ion at 60°, was investigated by the same procedure as for the corresponding tosylate. The reaction was studied for two concentrations. In the first case, 0.2781 g (0.0010 mol) of the sulfonium salt was dissolved in 50 ml of 0.2 M NaOH. The precipitate obtained had a weight of 0.1246 g.

In the second case, 2.7800 g (0.0100 mol) of the sulfonium salt was dissolved in 50 ml of water, and allowed to react with 50 ml of 0.2 M NaOH; the precipitate had a weight of 1.3180 g. In both cases, the tlc and the visible and ultraviolet spectra were similar to those obtained from the corresponding tosylate. The analysis of the precipitates are given in Table XXIV, p 84.

Reaction of p-Nitrobenzyldimethylsulfonium Bromide in the Presence of Oxygen. The experiment was carried out in a manner identical to that of the corresponding tosylate in the presence of oxygen. p-Nitrobenzyldimethylsulfonium bromide, 0.2784 g (0.0010 mol), was dissolved in 50 ml of distilled water, and allowed to react with 50 ml of 0.2 M NaOH; the precipitate obtained weighed 0.0924 g, and had a similar tlc, and visible and ultraviolet spectra to the precipitate obtained from the reaction of the corresponding tosylate in the presence of oxygen. The filtrate was shown to contain both p-nitrobenzyl alcohol, and p-nitrobenzaldehyde, but was not analyzed further. The analysis of the precipitate is given in Table XXIV, p 84.

Reaction of p-Nitrobenzyldimethylsulfonium Bromide in the Presence of Di-t-butyl Nitroxide. The experiment was preformed in a manner identical to that of the corresponding tosylate, except that a greater amount of the nitroxide was used. p-Nitrobenzyldimethyl-sulfonium bromide, 0.2779 g (0.0010 mol), and 0.1500 g (0.0010 mol) of di-t-butyl nitroxide were dissolved in 50 ml of water (the nitroxide was only partially soluable), and allowed to react with 50 ml of a 0.2 M NaOH solution. The appearance of the reaction

mixture was identical to that of the corresponding tosylate, except that less precipitate had formed after 4 hr. The resulting white precipitate weighed 0.0664 g; it was shown to consist of only one component, with the same R_f value as trans-p,p'-dinitrostilbene oxide. The visible and ultraviolet spectra shown only one band, with λ_{max} = 290 nm (DMF). The analysis of the precipitate is given in Table XXIV, p 84.

The filtrate contained some unreacted nitroxide, p-nitrobenzaldehyde, p-nitrobenzyl alcohol (the major component), and several unidentified products; it was not analyzed further.

Reaction of p-Nitrobenzyl Tosylate and Hydroxide Ion. p-Nitrobenzyl tosylate 0.3071 g (0.0010 mol), was dissolved in 50 ml of dioxane; the reaction was initiated by the addition of 50 ml of 0.2 M NaOH. After 24 hr, the reaction mixture was neutralized by the addition of dilute HCl, diluted to 500 ml with distilled water, and stored for 24 hr in a refrigerator. The precipitate was isolated by filtration, and dried for 4 hr at 50° and 2 torr. The light yellow precipitate weighed 0.0473 g; the tlc is given in Table XXXII. The amount of p,p'-dinitrostilbene, and cis- and trans-p,p'-dinitrostilbene oxides were determined by comparison of the area of the spots on the chromatogram to those of a series of spots from known solutions. The precipitate was recrystallized from acetic acid; two crops were obtained. The first crop, mp 195-196°, was recrystallized from ethyl acetate; the melting point alone and mixed, were identical with an authenic sample of trans-p,p'-dinitrostilbene

Table XXXII

Precipitate from the Reaction of p-Nitrobenzyl Tosylate and Hydroxide Ion

R_f Value	Estimated Amount**
0.00	small
0.20	trace
0.30	major
0.42	major
0.56*	significant
0.67	significant

Comparison of Standard Compounds

R_f Value	Compound
0.30	cis-p,p'-dinitrostilbene oxide
0.41	trans-p,p'-dinitrostilbene oxide
0.55*	cis- and trans-p,p'-dinitrostilbene

*Gave a yellow fluorescence with a long wave U.V. lamp (366 nm)

**major > large > significant > small > trace

oxide. The second crop, mp 140-150°, was recrystallized from dioxane--water, and had a melting point, alone and mixed, identical to that of an authentic sample of cis-p,p'-dinitrostilbene oxide.

The filtrate was extracted (3 x 50 ml) with methylene chloride; the organic layer was dried (Na_2SO_4), and the solvent completely removed. The resulting residue, 0.1190 g, was 67.3% p-nitrobenzyl alcohol (0.0800 g; 52.3% yield), 2.5% p-nitrobenzaldehyde (0.0030 g, 2.0% yield), and 0.2% p-nitrotoluene (trace). The Smiles's test[78]* on the residue was inconclusive for p-toluenesulfinic acid. The complete analysis is given in Table XXV, p 91.

Reaction of p-Nitrobenzyl Bromide. p-Nitrobenzyl bromide, 0.4320 g (0.0020 mol), was dissolved in 100 ml of dioxane, and allowed to react with 100 ml of 0.2 M NaOH. The reaction mixture was neutralized with dilute HCl after 24 hr; the solution was diluted with an equal volume of water, and cooled for 24 hr. The yellow precipitate, 0.0660 g, was isolated by filtration, washed with distilled water, and dried for 4 hr at 50° and 2 torr. The tlc of the precipitate gave a major spot with the same R_f value as p,p'-dinitrobibenzyl ether; small spots were observed that had the same R_f value as p,p'-dinitrostilbene and trans-p,p'-dinitrostilbene oxide (the cis-p,p'-dinitrostilbene oxide had almost the same R_f value as p,p'-dinitrobibenzyl ether), and were estimated by tlc, using a series of known solutions. The p,p'-dinitrobibenzyl ether was determined

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*The Smiles's test is specific for sulfinic acids. The compound is dissolved in concentrated sulfuric acid, and a drop of anisole or phenetole is added; a blue color developes if a sulfinic acid is present.

by glc; the precipitate was 21.0% p,p'-dinitrobibenzyl ether (0.0140 g, 4.9% yield).

The filtrate was extracted (3 x 50 ml) with chloroform; the organic layer dried (Na_2SO_4), and the solvent completely removed. The residue (0.2311 g) was 1.5% p-nitrotoluene (trace), 1.3% p-nitrobenzaldehyde (trace), 0.7% unreacted p-nitrobenzyl bromide (trace), and 88.3% p-nitrobenzyl alochol (0.2040 g; 66.7% yield). The complete analysis is given in Table XXVII, p 94.

Reaction of p-Nitrobenzyl Bromide in the Presence of Oxygen. p-Nitrobenzyl bromide, 0.4320 g (0.0020 mol), was dissolved in 100 ml of dioxane. A slow stream of oxygen was bubbled through the solution for 15 min, followed by the addition of 100 ml of 0.2 M NaOH. The flow of oxygen was discontinued after 15 min. The reaction mixture was neutralized with dilute HCl, and worked up in the same manner as previously described; 0.0572 g of a white precipitate was obtained. Analysis of the precipitate by tlc showed that it consisted of approximately equal amounts of two components: the two components had identical R_f values as cis- and trans-p,p'-dinitrostilbene oxides.

The filtrate was extracted (3 x 50 ml) with chloroform; the organic layer was dried (Na_2SO_4), and the solvent completely removed. The residue, 0.2440 g, was 96% p-nitrobenzyl alcohol (0.2340 g; 76.5% yield), and 4.0% p-nitrobenzaldehyde (0.0098 g; 3.2% yield). The complete analysis is given in Table XXVIII, p 95.

Reaction of p-Nitrobenzyl Iodide and Hydroxide Ion. The reaction of p-nitrobenzyl iodide was investigated in the same manner as

p-nitrobenzyl bromide. p-Nitrobenzyl iodide, 0.5361 g (0.0020 mol), was dissolved in 100 ml of dioxane; the reaction was initiated by the addition of 100 ml of 0.2 M NaOH. The light yellow precipitate obtained had a weight of 0.6000 g; the tlc of the precipitate was almost identical to that of the precipitate from the bromide. The residue from the extraction weighed 0.3212 g; it was 76.2% p-nitrobenzyl alcohol (0.2442 g; 80.0% yield), and 2.1% p-nitrobenzaldehyde (0.0067 g; 2.2% yield). The products were not further analyzed.

APPENDIX A

Calculations of Kinetic Isotope Effects

To obtain the relationship between the chlorine kinetic isotope effect and the experimentally obtained ratio of Cl_{37} to Cl_{35}, it is necessary to consider the two reactions:

$$2\ ArCH_2Cl + 2\ OH^- \rightarrow ArCH{=}CHAr + 2\ Cl^- + 2\ H_2O \qquad (107a)$$

$$2\ ArCH_2Cl' + 2\ OH^- \rightarrow ArCH{=}CHAr + 2\ Cl'^- + 2\ H_2O \qquad (107b)$$

Where Cl and Cl' refer to Cl_{35} and Cl_{37}, respectively. The two equations may be summarized as follows:

$$R \xrightarrow{k_{35}} P \qquad (108a)$$

$$R' \xrightarrow{k_{37}} P' \qquad (108b)$$

In these two equations, R and R' stand for the two isotopically different species of p-nitrobenzyl chloride (the reactant), and P and P' stand for the ionic chloride (the product). The rate expressions for these equations are:

$$-\,dR/dt = k_{35}\,R \qquad (109a)$$

$$-\,dR'/dt = k_{37}\,R' \qquad (109b)$$

It is understood that the symbols R and R' represent the concentrations; the brackets are omitted for simplicity. Dividing equation

109a by equation 109b gives:

$$\frac{dR}{dR'} = \frac{k_{35}R}{k_{37}R'} \tag{110}$$

Equation 110 is rearranged and integrated between the limits of the initial and final concentrations of the two isotopes.

$$\int_{R_o}^{R} \frac{dR}{R} = \frac{k_{35}}{k_{37}} \int_{R'_o}^{R'} \frac{dR'}{R'} \tag{111}$$

$$\ln(\frac{R}{R_o}) = \frac{k_{35}}{k_{37}} \ln(\frac{R'}{R'_o}) \tag{112}$$

For the concentration R, at any time, the following relationship holds: $R = R_o - P$, and similarly $R' = R'_o - P'$. Substitution and rearrangement gives:

$$\ln\ (1 - \frac{P}{R_o}) = \frac{k_{35}}{k_{37}} \ln\ (1 - \frac{P'}{R'_o}) \tag{113}$$

If the reaction is quenched at an early stage, then the ratio of product to reactant (P/R_o) is a small number. Therefore, one can use the approximation, $\ln\ (1 - x) \cong -x$.

$$\ln\ (1 - \frac{P}{R_o}) \cong - \frac{P}{R_o} \tag{114a}$$

$$\ln\ (1 - \frac{P'}{R'_o}) \cong - \frac{P'}{R'_o} \tag{114b}$$

Making these substitutions into equation 113 gives:

$$\frac{P}{R_o} = \frac{k_{35}}{k_{37}} \left(\frac{P'}{R'_o}\right) \tag{115}$$

Rearrangement of equation 115 gives equation 63 (on page 38).

APPENDIX B

Gas Liquid Chromatography

The identity of the compounds in this work were verified by glc analysis on a 5% SE-30 column. Due to the wide range of melting points encountered (over a 250° range), it was not possible to determine all the products at one temperature. The lower-melting compounds, which usually were recovered by extraction of the filtrates, were determined with a column temperature of 170°, with trans-stilbene as an internal standard. The higher-melting compounds, usually found in the precipitates, were usually determined with a column temperature of 270°, with N-benzhydrylideneaniline as an internal standard. It must be noted that trans-p,p'-dinitrostilbene was determined at 270°, which is below its melting point. However, it has a strong tendency to sublime at temperatures above 250°; the injection port was set at approximately 325°. The determination of the dinitrostilbene was not ideal at these conditions.

For some of the initial work, a Varian Aerograph Model P-90 gas chromatographic unit with a 5 ft x 0.250 in. SE-30 column was used. Compounds that had been tentatively identified by their retention times were verified by micro-preparative glc. This was accomplished by trapping some of the material at the exit port. The compounds were collected by attaching a 4 mm glass tube to the collector outlet, while the compound desired was passing through the detector. The material that condensed in the tube was washed onto a portion

of spectral grade KBr, using a small amount of chloroform. The chloroform was then removed from the KBr, by a brief drying of the sample in an oven, followed by preparation of a KBr pellet. p-Nitrobenzyl alcohol and p-nitrobenzaldehyde were verified by their infrared spectra in this manner. p-Nitrotoluene was verified by its ultraviolet spectrum, since the amount of the compound collected was too small for analysis by infrared.

Quantitative analysis was accomplished using a Varian Aerograph 600-D gas chromatographic unit with a flame ionization detector, and a 5% SE-30 6 ft x 0.125 in. column. Calibration curves for the following compounds were prepared with trans-stilbene as the internal standard: p-nitrotoluene, p-nitrobenzaldehyde, p-nitrobenzyl chloride, p-nitrobenzyl bromide, p-nitrobenzyl alcohol, and p-dinitrobenzene. The calibration curves were a plot of the area fraction (AF) of the compound vs the weight fraction (WF).[79] The area fraction is defined as the area of the peak of the compound divided by the area of the peak of the standard compound.

$$AF = \frac{\text{Area of compound's peak}}{\text{Area of standard's peak}} \tag{116}$$

The weight fraction is the ratio of the weights of the compound and the standard in the sample.

$$WF = \frac{\text{Weight of compound in sample}}{\text{Weight of standard in sample}} \tag{117}$$

The internal standard was chosen such that it has a retention time similar to the compounds being determined, but still gives complete

separation, and that it does not effect the chromatographic behavior of the components being determined. An example of a typical calibration curve is given in figure 8.

A sample calculation illustrating the internal standard method is given for the p-nitrobenzyl bromide-hydroxide ion reaction; a precipitate (0.0660 g) and a residue (0.2311 g) from extraction of the filtrate were isolated. The residue was analyzed by tlc and glc, and shown to contain mostly p-nitrobenzyl alochol, and lesser amounts of p-nitrobenzaldehyde, p-nitrotoluene, and unreacted p-nitrobenzyl bromide. A sample was prepared from the residue; the sample contained 0.0317 g of the residue and 0.0288 g of the internal standard. The information obtained is given in table XXXIII.

Table XXXIII

Analysis of the Residue from p-Nitrobenzyl Bromide Reaction[a]

Compound	Area	AF	WF	% Compound
p-nitrotoluene	4,480	0.0125	0.0167	1.5
p-nitrobenzaldehyde	2,200	0.0062	0.0140	1.3
p-nitrobenzyl bromide	1,400	0.0040	0.0076	0.7
p-nitrobenzyl alcohol	151,000	0.422	0.970	88.3
internal standard	358,000			

[a]Determined on a SE-30 column at a temperature of 170°, with trans-stilbene as the standard.

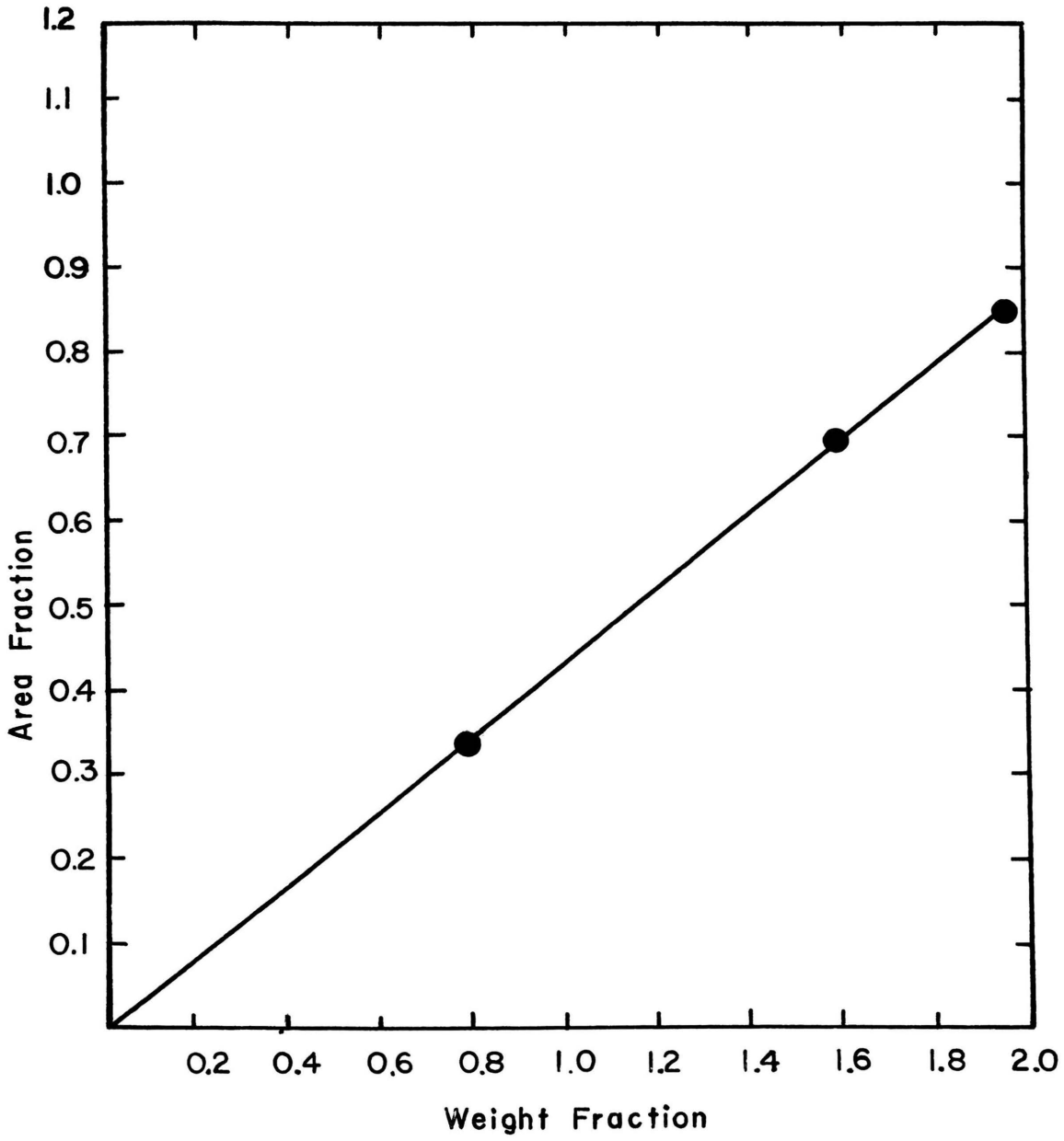

Figure 8. Plot of area fraction vs weight fraction for GC determination of p-nitrobenzyl alcohol

The % p-nitrobenzyl alochol was calculated as follows. The area fraction is obtained from the areas of p-nitrobenzyl alcohol and the internal standard.

$$AF = \frac{151{,}000 \text{ units}}{358{,}000 \text{ units}} = 0.422 \qquad (118)$$

The weight fraction is then obtained from the appropriate calibration curve (fig 8); the area fraction of 0.422 corresponds to a weight fraction of 0.97. From the definition of the weight fraction, one obtains the weight of p-nitrobenzyl alcohol in the sample prepared.

$$WF = \frac{\text{weight of p-nitrobenzyl alcohol in sample}}{\text{weight of internal standard in sample}} \qquad (119)$$

and

$$\% = \frac{\text{weight of p-nitrobenzyl alcohol in sample}}{\text{weight of residue in sample}} \times 100\% \qquad (120)$$

or

$$\% = \frac{WF \times \text{weight of internal standard}}{\text{weight of residue in sample}} \times 100\% \qquad (121)$$

Therefore, the percentage of p-nitrobenzyl alcohol in the sample is:

$$\% = \frac{(0.97)\ (0.0288\ g)}{(0.0317\ g)} \times 100\% = 88.3\% \qquad (122)$$

The other components in the residue were calculated in the same manner, using the appropriate calibration curve.

In some instances, the analyses were accomplished by calculating a response factor (RF) instead of constructing a calibration curve.

If the calibration curve is linear, then the response factor is just the slope of the curve.

$$RF = \frac{AF}{WF} \tag{123}$$

The precipitate from the p-nitrobenzyl bromide reaction (0.0660 g) was analyzed for p,p'-dinitrobibenzyl ether (BBE), using the measured response factor for that compound; N-benzyhydrylideneaniline was the internal standard. The values in the following table are used to illustrate this calculation.

Table XXXIV

Analysis of the Precipitate from p-Nitrobenzyl Bromide Reaction[a]

Component	Weight	Area	AF	WF
p,p'-dinitrobibenzyl ether	7.0 mg	6,430	0.125	0.538
internal standard	12.0 mg	51,200		
precipitate	4.8 mg	1,920	0.0256	0.12
internal standard	8.4 mg	75,300		

[a]Determined on a SE-30 column at a temperature of 250° with N-benzhydrylideneaniline as the internal standard.

The response factor, 0.215, is obtained from the ratio of the area fraction to the weight fraction for the standard sample.

$$RF = \frac{0.125}{0.583} = 0.215 \tag{124}$$

The response factor is then used to calculate the weight fraction for the unknown sample, from the area fraction measured.

$$WF = \frac{AF}{RF} \tag{125}$$

$$WF = \frac{0.0256}{0.215} = 0.12 \tag{126}$$

The composition of the precipitate was then determined to be:

$$\%_{BBE} = \frac{(0.12)\ (8.4\ mg)}{(4.8\ mg)} \times 100\% = 21\% \tag{127}$$

APPENDIX C

Thin Layer Chromatography

Plates for thin layer chromatographs were prepared by spreading the adsorbent on 20 x 20 cm glass plates with a Desaga applicator, set at a thickness of 0.25 mm. The slurry of the adsorbent was prepared by adding approximately 65 ml of water to 30 g of Brinkmann Silica Gel HF-254. The plates were allowed to dry overnight, followed by a 30-min drying period in a 110° oven. The compounds were spotted on the plate from an acetone solution of approximately 1 mg of the compound per 1 ml of solvent. The amount applied varied; 5-10 lambda (5-10 μg of the compound) of the solution were typically used. For detection of trace amounts of a compound in a mixture, a heavier application was necessary. The plates were developed for a distance of 10 cm in a standard chromatographic tank, lined with chromatographic paper, using benzene as the solvent (except where otherwise noted). The plates were scored at a distance of 10 cm above the spot of application, and were removed when the solvent front had completely reached the mark. It was observed that if the plates were left for an additional period of time, the R_f values were altered. Because the R_f values are never completely constant, standard samples of known compounds were run alongside all unknown mixtures.

The chromatograms were viewed with the aid of a short-wave ultraviolet lamp in a dark room. The phosphor in the adsorbent,

causes the spots to appear dark against a light background. p,p'-Dinitrostilbene could be conveniently visualized using a long-wave ultraviolet lamp; the compound gives a bright yellow fluorescent spot, even in very low concentrations. Most other compounds observed did not exhibit a similar fluorescence. In a few cases, it was convenient to spray the plate with reagents to aid in the visualization or identification of compounds after the plate had been developed. Acidic compounds, such as p-nitrobenzoic acid or p-toluenesulfonic acid, were visualized by spraying with a dilute solution of Lacmoid indicator in ethanol. The acidic spots appear pink against a blue background. If silica gel containing a phosphor was not available, the plates were sprayed with a dilute solution of the sodium salt of fluorescene in water, and observed with a short-wave ultraviolet lamp.

Preparative tlc was accomplished by spotting a continuous heavy band of the material about 1 cm from the bottom edge of the plate. The layer was developed the full distance of the plate to get maximum separation of the bands. The parts of the layer containing the band of the compound of interest, were scraped off using a razor blade. The compound was leached away from the adsorbent, using chloroform containing a small amount of methanol. The solvent was then removed by stripping on a rotary evaporator.

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VITA

Paul Henry Ruehle was born April 2, 1938 in Chatham, New Jersey. He received his elementary and early secondary education in Kirkwood, Missouri. He attended New Mexico Military Institute at Roswell, New Mexico, and graduated from high school in 1956. He received his Bachelor of Arts degree in Biology from Central Methodist College at Fayette, Missouri in 1961. He taught chemistry and physics at Warrenton High School, Warrenton, Missouri from 1961 to 1966. He attended NSF Summer Institutes for High School Teachers at the University of Missouri at Rolla in 1963, 1964, and 1965; he received the degree of Masters of Science for Teachers in August 1966. In September, 1966, he entered the University of Missouri at Rolla to study for the degree of Doctor of Philosophy in Chemistry. In 1973, he held a position of lecturer at Monmouth College, at Monmouth, Illinois.